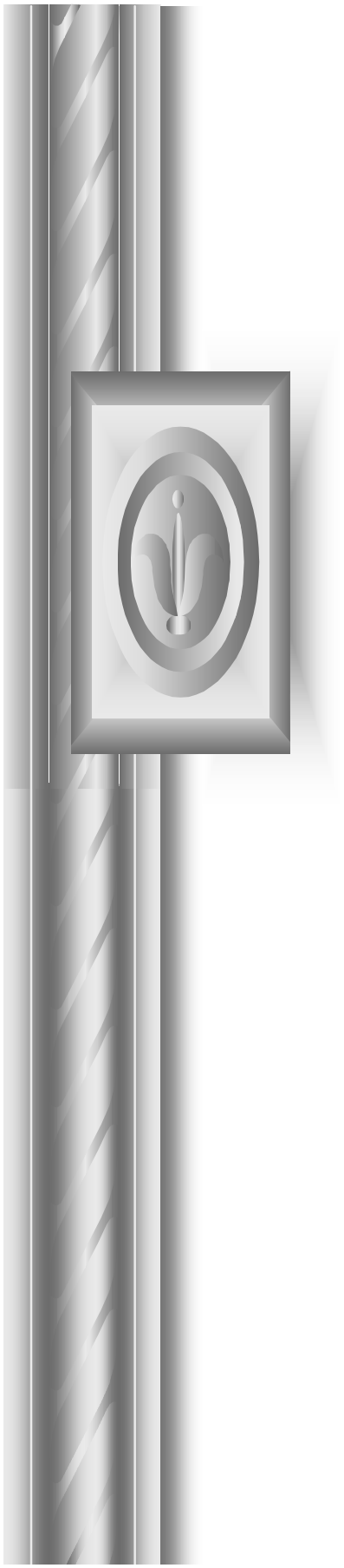

National Institute on Aging

Guide to Research and Training Programs

July 2001

Navigating the Guide

The *NIA Guide to Research and Training Programs, July 2001*, is the fifth edition of the Guide developed by the Office of Planning, Analysis, and Evaluation. Its purpose is to provide an introduction to the organization, major research topics, awards and award mechanisms of the National Institute on Aging (NIA). Each year the Guide is updated to reflect NIA's most recent scientific advances and research opportunities. The *Introduction* to the Guide presents a brief overview of the NIA and its major research advances. The next two sections describe the broad spectrum of research interests and initiatives supported by NIA's research programs. It includes a summary of the collaborative activities undertaken by the NIA and its federal research partners. These sections are followed by summaries of administrative activities, including scientific review of extramural and intramural research, scientific planning, public information services, international research activities, and NIA's interactions with the U.S. Congress. The remainder of the Guide provides information on NIA's budget and research support mechanisms. A list of contacts is provided so readers can gain additional and/or updated information on the NIA programs and research opportunities. To assist the reader, the Guide also contains a list of frequently used acronyms and a glossary of commonly used terms.

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NIA's Challenge for the Future

During the 20th century, life expectancy in the U.S. increased from less than 50 years to more than 76 years. The challenge for the 21st century will be to make these added years of life as healthy and productive as possible.

By the year 2011, 75 million baby-boomers, people born between 1946 and 1964, will begin to turn 65. By 2050, the number of Americans over the age of 65 will double, and the number of Americans over age 85 will increase five-fold or more, placing a significantly greater number of people at risk for disease and disability. It is urgent to develop more effective treatments for age-related diseases, including Alzheimer's disease (AD), heart and vascular diseases, and cancer, and to prevent or delay the onset of disease and disability. With today's older population accounting for about a third of the estimated $1 trillion in U.S. health expenditures, the need to conduct research that leads to more effective treatments for the diseases common in later years, and the need to develop interventions to prevent disabilities among older persons has never been greater.

Highlights of Progress in Aging Research

When the NIA was first established, gerontology was a young science. Now, aging research is on the threshold of a new era of scientific discoveries with great potential for preventing disease and disability and for promoting health in later years. The following descriptions give selected examples of recent NIA-funded research developments.

Alzheimer's disease. Alzheimer's disease is the most common cause of dementia in the U.S. It affects as many as 4 million Americans; the associated costs to individuals and to public programs are estimated at greater than $100 billion per year. As the primary federal agency responsible for research on Alzheimer's disease research, the NIA leads national efforts to gain greater understanding of the biological mechanisms underlying the disease process and to develop preventive measures and treatments. As a result of intense research activity, scientists have produced an extraordinary body of knowledge relevant to AD. Building on basic research findings, major advances were reported this year on two potential intervention strategies. One study identified a key enzyme involved in the formation of amyloid and the other focuses on stopping the development of amyloid plaques by immunization.

Early pathologic changes in the brain, including the formation of amyloid deposits and neurofibrillary tangles, are believed to play a causative role in AD. Amyloid is a small peptide fragment produced as a result of snipping (cleavage) of the much larger amyloid precursor protein (APP) by two enzymes known as beta (β) and gamma (γ) secretase. For years, scientists knew that something was snipping the APP into fragments and they even went so far as to name the suspect secretases. But no one had been able to physically and precisely identify the enzymes that did the actual clipping of APP until the past year, when the identities of the β and γ secretases at last were revealed.

The identity of β secretase was discovered simultaneously by several drug companies. However, γ secretase has proven more elusive. Its activity was known to be affected by mutations in one of the genes (presenilin 1 or PS1) that cause AD in early onset families.

PS1 was identified several years ago and structural evidence suggested it might actually be the γ secretase. To test this possibility, scientists identified a radioactive molecule that binds tightly to the active site of the enzyme, thus labeling the enzyme molecules. They found that PS1 was the labeled protein, strongly suggesting that it itself is the γ secretase. It is believed this line of research could lead to the discovery of drugs that inhibit the production of amyloid without inhibiting other essential functions these secretase enzymes might have. Ultimately, clinical trials on such secretase-inhibiting drugs will show whether this approach will work.

In another exciting development, pharmaceutical company scientists showed that repeated long-term injections of an amyloid vaccine can cause an immune response in a transgenic mouse model, nearly eliminating amyloid plaques and associated neuropathology, with no obvious toxicity. A number of NIH-funded scientists have confirmed and extended these observations. In a novel approach, one group administered the vaccine to mice nasally, and also induced an immune response. The mice had a much lower amyloid burden at middle age than animals not receiving the vaccine. Interest in the vaccine approach heightened upon recent preliminary reports that amyloid vaccination prevents cognitive decline in another transgenic mouse model of AD, suggesting that a vaccine might indeed make a difference in the clinical symptoms of AD. Human trials are only now beginning to test both the safety and the efficacy of these vaccines as a possible therapy for people with AD.

In addition, work is continuing on the Memory Impairment Study, the first AD prevention clinical trial carried out by NIH, which was launched by the NIA in 1999. This study, targeting individuals with mild cognitive impairment (MCI), is being conducted at more than 70 sites across the U.S. The trial compares the effects of vitamin E and donepezil (brand name Aricept) in preventing the development of AD in people diagnosed with MCI, a condition found to be the likely precursor of AD. Ongoing trials are also examining the effectiveness of naproxen and celecoxib (anti-inflammatory drugs) in reducing the risk of AD in persons with a family history of dementia, the effect of estrogen replacement therapy in preventing AD in women with a family history of the disease, and whether treatment with a variety of agents, such as aspirin, vitamin E, antioxidants, or combined folate/B6/B12 supplementation can prevent older women from developing age-related memory impairment or AD.

Reducing frailty and disability. As life expectancy increases, there is an ever greater need to keep these additional years disease and disability-free. According to a 1999 report by the U.S. National Center for Health Statistics (NCHS), some 79 percent of people age 70 and older have at least one of seven potentially disabling chronic conditions (arthritis, hypertension, heart disease, diabetes, respiratory diseases, stroke, and cancer). However, positive results from a 1997 study by Kenneth Manton and colleagues found that disability levels for people age 65 and older have actually been falling since 1982, and that the increase between 1982 and 1994 in the number of older Americans with chronic functional limitations was less than half of the increase that might have been expected. Subsequent findings have shown that the benefits of this trend extend to both men and women and to minority groups. The core findings from Manton's study were reaffirmed in a 1998 RAND study that found reductions in disability rates in every age group and for every functional measure, with the largest improvements in people age 80 and older. Ultimately, continuing research on a wide range of questions will provide a clearer understanding of how to continue the disability decline and will discern its implications for work, caregiving, living arrangements, health and

long-term care costs, and other areas of social and economic well-being. NIA research is helping to define optimal regimens regarding diet, diet supplements, exercise, safety, and other factors to ensure that endurance, strength, and balance are kept at the highest possible levels and that the risks of disease and disability are minimized.

Recent studies in older adults have shown that exercise in four key areas – endurance, strength, balance, and flexibility – can improve function and reduce disease. Endurance exercise improves function of the heart, lungs, and circulatory system, and may help prevent heart disease, diabetes, stroke and colon cancer. Strength exercises help prevent osteoporosis, and balance and flexibility exercises help prevent falls and other injuries. Even in adults over age 85, exercise builds muscles, increases metabolism, and helps keep weight and blood sugar at proper levels. In another study of men 30-83 years of age, investigators found that it is fitness, not fat, that is most important for overall health and decreased risk of chronic disease and death. Not surprisingly, the study showed that the higher the level of fat, the lower the level of fitness; however, within each category of body fat, "fit" men were at lower risk of death. Most strikingly, among those more fit, obesity was not significantly related to risk of death. These findings suggest that, focusing on fitness rather than weight-loss to prevent conditions most often associated with obesity may be more beneficial for those patients who are by definition, clinically obese.

Biology of aging and the genetics of longevity. Aging is accompanied by gradual changes in most body systems. Research on the biology of aging focuses on understanding the cellular and molecular processes underlying these changes, as well as those accompanying the onset of age-related diseases. In mammals, there is a progressive physiologic decline with aging that is often accompanied by disease and disability. NIA studies have begun to reveal the biologic factors associated with extended longevity, implicating numerous genes in normal aging processes, age-related pathologies and diseases, and longevity. Some of these genes are associated with dramatic extension of life span. A new initiative will extend studies of longevity-associated genes, changes in gene expression patterns, and the genetic epidemiology of human longevity. The ultimate goal of this effort is to develop interventions to reduce or delay age-related degenerative processes in humans. Studies can help identify the relative contributions of environment and heredity to dementia, cognitive abilities, physical functioning, well-being, and social aging. New techniques can track the developmental course of genetic contributions to behavior, identify genetic heterogeneity, and explore genetic links between the normal and abnormal. In addition, basic research will explore error accumulation in DNA with age and how the cell repairs such damage.

Osteoporosis. Loss of bone mass due to osteoporosis results in about 1.5 million fractures each year in the U.S., and causes substantial pain, dysfunction, and death in later life. Once thought to be a normal part of aging, osteoporosis is now known to be largely preventable. Several institutes at NIH, including NIA, NIAMS, NIDCR and NIDDK, support both basic and clinical studies of the mechanisms of bone loss, and the development of therapeutic agents to slow or ameliorate the progression of bone loss. In a recently completed study of women from the Study of Osteoporotic Fractures (SOF), higher blood pressure was found to be associated with decreased bone density at the femoral neck. This association may reflect the fact that hypertension is associated with abnormalities in calcium metabolism, and may contribute to an enhanced risk of hip fractures. Preventive and treatment strategies that can control high blood pressure (such as restriction of sodium intake and thiazide diuretics) and

reduce calcium loss should be explored further for their ability to reduce bone loss and prevent osteoporotic fractures.

Several therapies (including calcium and vitamin D, estrogen, calcitonin, and the newly FDA-approved alendronate, raloxifene, risedronate) are efficacious in stemming bone loss, producing modest gains in bone mineral density and preventing fractures. However, the ability to markedly stimulate bone formation and increase bone mass is very limited. Recent findings suggest that combination therapies such as a) estrogen + calcium + vitamin D, b) alendronate + estrogen, c) PTH + estrogen and d) estrogen + calcitriol may produce additive (or synergistic) effects resulting in more substantial gains in bone density.

Cardiovascular disease. Cardiovascular disease (CVD) affects nearly 60 million Americans and is a main cause of disability and the leading cause of death of Americans 65 years of age and older. Although age is a major risk factor for CVD, the reasons remain unclear. To better appreciate the link between aging and development of disease, we need to better understand normal aging; i.e., aging in the absence of disease, and how aging impacts on the development of CVD in older persons. The NIA has a major interest in understanding the importance of blood vessel stiffening in aging and in the development of cardiovascular disease. The ultimate goal of this research is to identify preventive strategies (e.g., modification of risk factors through exercise and/or dietary interventions) or new therapeutic strategies (e.g., novel drug development or even gene therapy) to prevent, delay, arrest, or even reverse blood vessel stiffening and its potentially harmful effects on the cardiovascular system. It has been found that the rise in systolic blood pressure and pulse pressure (the difference between systolic and diastolic pressure) in women from their pre-menopausal to their post-menopausal years is about two-fold greater than that observed in men over the same time period. Therefore, ascertaining the physiological factors that may modulate the rise of blood pressure with age in women is particularly important. Another study found that regular aerobic-endurance exercise likely prevents age-associated elevations in systolic blood pressure and pulse pressure – the two most important risk factors contributing to age-associated cardiovascular morbidity and mortality. Exercise training significantly reduced systolic and diastolic blood pressure by about 11%. These changes were accompanied by a significant reduction in left ventricular wall thickness.

Preventing disease through behavior change. Health behaviors include lifestyle selections in diet, smoking, exercise, social activity levels, and the use of health care services. The links between health and lifestyle are now indisputable. NIA health behavior research focuses on three related areas: 1) health practices and lifestyle factors predicting functioning, morbidity and mortality; 2) disease recognition and management of chronic illnesses and disabilities; and 3) the development and testing of theory-based behavioral interventions. Current efforts are concentrated in the area of physical activity and exercise research. NIA is funding studies to determine the functional effects of different types of exercise training programs (i.e., strength, endurance, balance and flexibility) on various physical functioning and psychosocial health outcomes, and to characterize the personality and motivation of people most likely to adhere to exercise regimens. Recent studies found that the most common barriers to physical activity include caregiving duties, lack of time, and lack of energy. To adequately design effective physical activity programs, it is necessary to understand factors that promote or impede regular physical activity.

Behaviorally-based programs that rely on existing community programs have been found to be effective in increasing physical activity. A recently completed study recruited both intervention participants and a non-intervention control group to study the effectiveness of the Community Healthy Activities Model Program for Seniors (CHAMPS-II) in which participants explored personal barriers to exercise and designed an individually tailored plan for increasing physical activity. The 1-year intervention successfully increased physical activity levels by the equivalent of adding five brisk 1-mile walks per week. The intervention also resulted in a decrease in body mass of the intervention group. This study suggests that the CHAMPS II intervention and its use of individually tailored activities is an appropriate strategy for increasing physical activity among older adults. Reliance on existing community programs and structures helps ensure the long-term maintenance of older people's physical activity gains.

NATIONAL INSTITUTE ON AGING

Richard J. Hodes, M.D., Director

Introduction

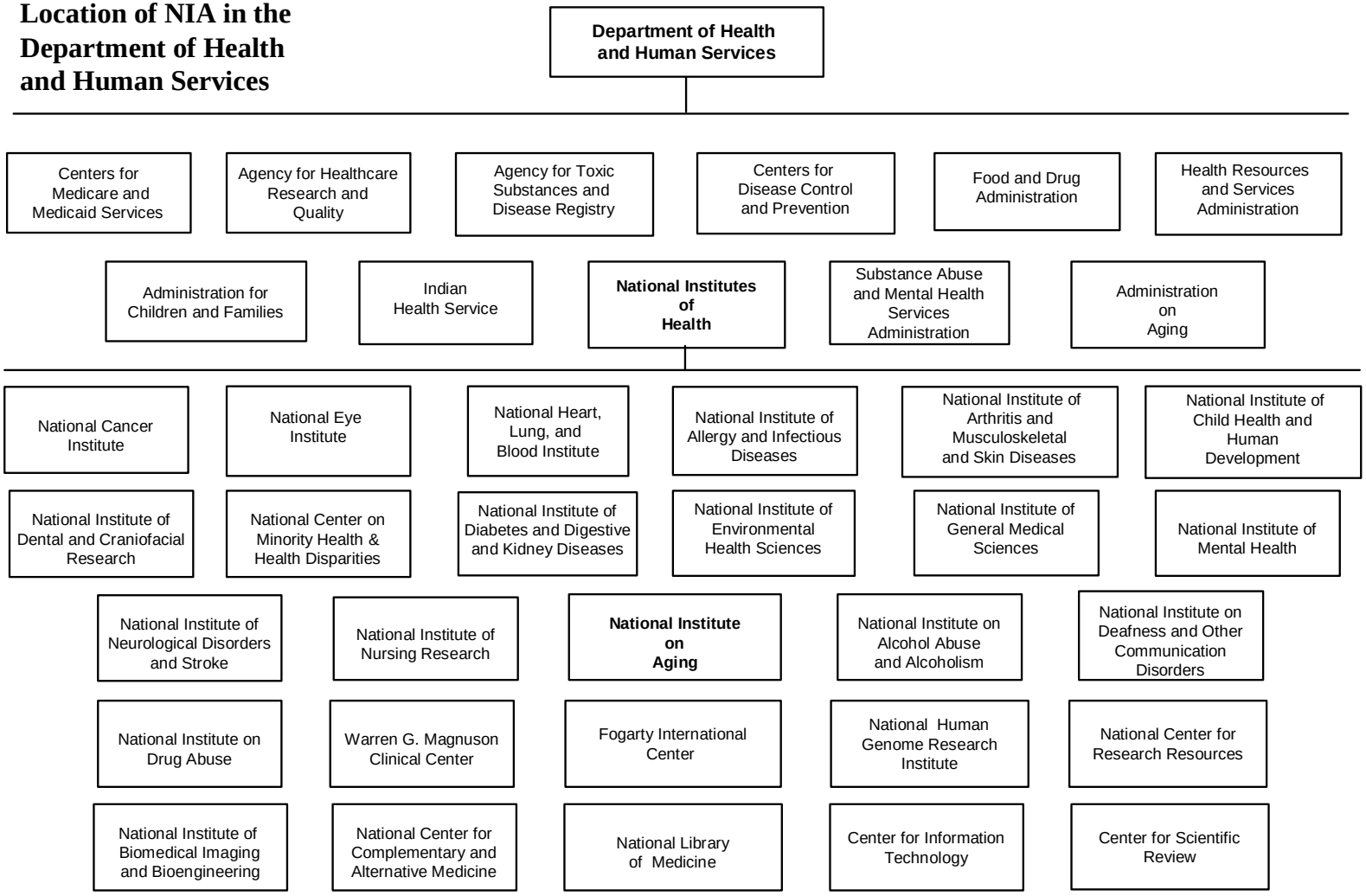
The National Institute on Aging (NIA), one of 27 institutes and centers of the National Institutes of Health (NIH), leads the federal effort on aging research. This enterprise has rapidly expanded knowledge about the biological, behavioral, and social changes that occur with advancing age; improved our understanding of the nature of aging; and extended the healthy, active years of life. Many of these advances have saved lives and prevented disability by contributing to improvements in public health and health care. Numerous findings have challenged stereotypes about the inevitability of decline in old age, generating effective strategies that can maintain or even enhance both physical and cognitive abilities in old age. Other discoveries have provided exciting insights into the secrets of aging and longevity. These successes benefit all generations.

The NIA is committed to addressing racial and ethnic issues, both with respect to appropriate scientific questions within individual studies, and with respect to encouraging training of minority investigators. The NIA is dedicated to training the next generation of investigators to continue achievements in aging research, and is providing resources for an efficient and effective research infrastructure. The Institute maintains an award-winning program to communicate the results of aging research and related health information to the research community, health care providers, patients, and the general public, providing guidance on health care, health promotion, and disease prevention for older people.

NIA Mission

- Support and conduct research on:
  - aging processes
  - age-related diseases
  - special problems and needs of the aged
- Train and develop research scientists
- Provide research resources
- Disseminate information on health and research advances

Location of NIA in the Department of Health and Human Services



Revised 6/01

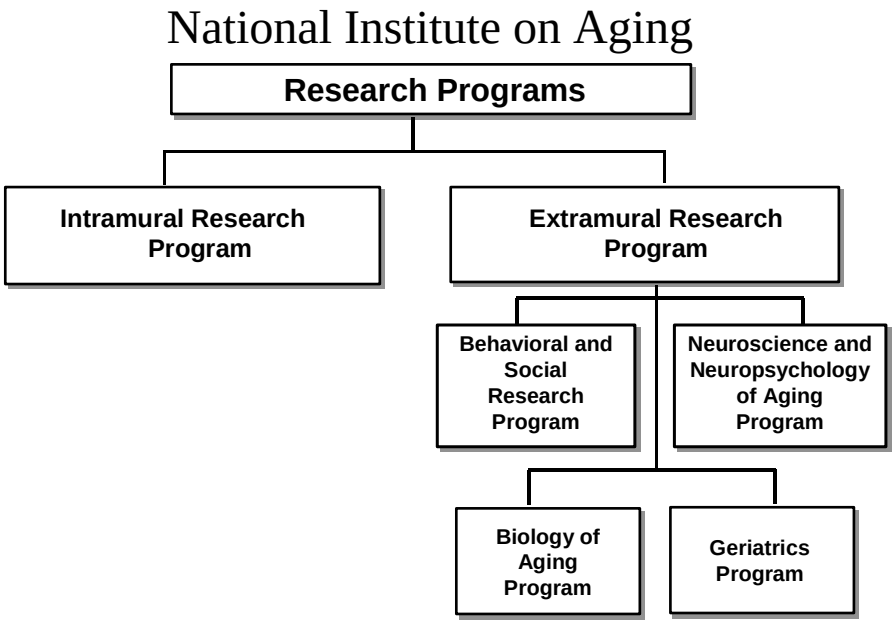
NIA RESEARCH PROGRAMS

Richard J. Hodes, M.D., Director

Program Organization

The National Institute on Aging (NIA) includes both extramural and intramural research programs. The four extramural programs are the Biology of Aging Program, the Behavioral and Social Research Program, the Geriatrics Program, and the Neuroscience and Neuropsychology of Aging Program. The Intramural Research Program is comprised of ten research laboratories, and a research resources branch.

The Extramural Research Program funds research in universities and other research centers across the country and, in selected circumstances, internationally. It also supports training of future research scientists. The NIA issues Program Announcements (PA) intended to focus research grant applications on scientific areas of interest to the NIA. Requests for Applications (RFA) are issued by the Institute when research is needed on specific topics of major importance to the Institute, and includes a budget set-aside. The extramural programs also conduct workshops and other activities to identify promising areas for NIA-supported research and coordinate the development of research initiatives. NIA intramural scientists conduct basic and clinical research on the NIH campus in Bethesda, MD, and in Baltimore, MD, at the Gerontology Research Center, site of the 41-year-old Baltimore Longitudinal Study of Aging.



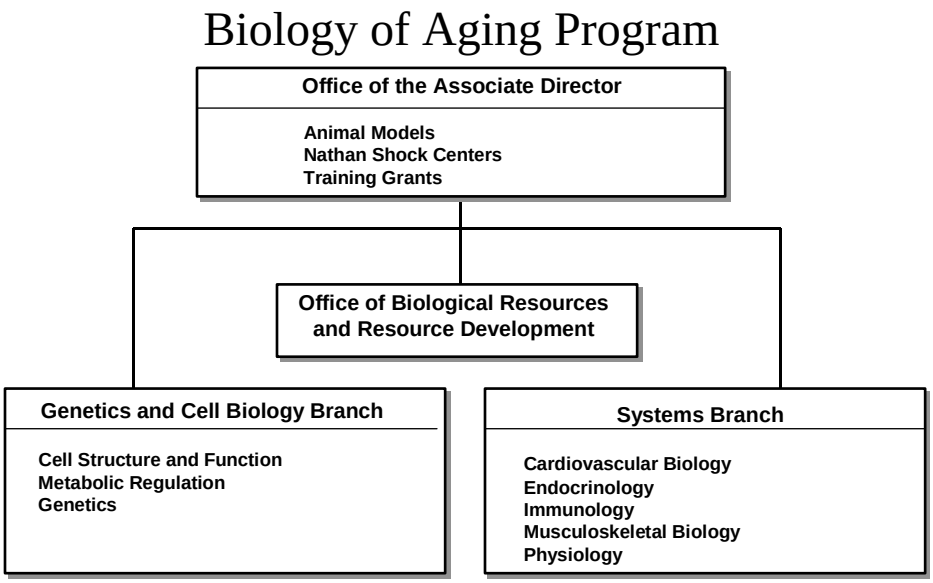
BIOLOGY OF AGING PROGRAM

Huber R. Warner, Ph.D., Associate Director
(*For further information, contact* BAPquery@nia.nih.gov*)*

The **Biology of Aging Program (BAP)** plans, implements, and supports molecular, genetic, cellular, and physiological research on mechanisms of normal aging and age-related pathologies. The overall objective of BAP's programs is to elucidate the biochemical, genetic and physiological mechanisms of aging and age-related changes in humans and animal models. This includes investigations of the gradual or programmed alterations of structure and function that characterize normal aging, as well as investigations of the adverse changes that are risk factors for or accompany age-related disease states.

Although the research emphasis in BAP is on aging in mammals, lower organism (*e.g. Drosophila, C. elegans*, yeast) research that is related to aging is also supported. The value of the comparative approach in studying aging has been well demonstrated by the Longevity Assurance Gene (LAG) Interactive Network of investigators, and the insights they are providing about the genetic basis of aging in humans.

The Program also includes the Office of Biological Resources and Resource Development (OBRRD) which coordinates the acquisition, maintenance and provision of resources supporting aging research, including cell and tissue banks, aged rodent colonies and non-human primate models.



DESCRIPTION OF BAP GRANT PROGRAMS

Office of the Associate Director

Huber R. Warner, Ph.D., Associate Director

Animal Models Program - *Nancy L. Nadon, Ph.D.* The objective of the Animal Models Program is to identify and develop new animal models, both mammalian and lower organism, for use in aging research. These models include rats, mice, rabbits, non-human primates, insects, nematodes and yeast. Mutant and genetically-engineered rodent models of both normal aging and specific age-related pathologies are of particular interest.

Nathan Shock Centers for Excellence in the Basic Biology of Aging - *Huber R. Warner, Ph.D.* This Core Center Grant program (P30 mechanism) was established in 1995 to enhance well-developed institutional programs in basic research on aging by providing state-of-the-art research resources to create the strongest environment possible for the conduct of basic aging research. Applications are accepted only in response to a Request for Applications (RFA).

Training Grant Program - *Huber R. Warner, Ph.D.* NIA recognizes a continuing and expanding need to train new researchers in aging research, and the institutional training grant program is the major mechanism for accomplishing this. Training grants provide individual and institutional support for graduate students and post-doctoral fellows. Support for individual trainees is usually limited to 3 years.

Genetics and Cell Biology Branch

Anna McCormick, Ph.D., Chief

Cell Structure and Function Program - vacant, recruitment in progress

The objectives of the Cell Structure and Function Program are to support research on the molecular basis of age-related changes in:

- Signal transduction mechanisms
- Microenvironment/extracellular matrix
- Cell senescence/apoptosis/cancer
- Membranes and membrane receptors

Metabolic Regulation Program - *David Finkelstein, Ph.D.*

Areas of investigation in the Metabolic Regulation Program include:

- Nutrition/metabolism
- Age-related changes in mitochondrial function/mitochondrial dysfunction
- Mechanism of life span extension by caloric restriction
- Generation of free radicals and oxidative stress

Genetics Program - *Anna McCormick, Ph.D.*

The objectives of the Genetics Program are to support research on:

- Identification and characterization of longevity assurance genes (LAGs) and senescence assurance genes (SAGs)
- Genome stability
- Genomics
- Mouse mutagenesis
- Single nucleotide polymorphisms/genetic epidemiology
- Telomere biology
- Werner's syndrome

Protein Structure and Function Program – *Frank Bellino, Ph.D.*

- Age-related post-translational modifications
- Formation of protein aggregates
- Protein turnover

Systems Branch

Jill Carrington, Ph.D., Chief

Cardiovascular Biology Program - *David Finkelstein, Ph.D.*

The objectives of the Cardiovascular Biology Program are to support basic research on:

- Age-related changes in cardiovascular function
- Factors affecting cell death/cell division in cardiovascular tissue

Endocrinology Program - *Frank Bellino, Ph.D.*

The purpose of the Endocrinology of Aging program is to support basic molecular and cellular research into the causes and effects of age-related changes in the endocrine system. Areas of investigation in this program include:

- Age-related changes in hormone production, metabolism, and action
- Type II diabetes
- Reproductive aging
- Biology of menopause; animal models of menopause
- Age-related changes in control of prostate growth
- Endocrine aspects of age-dependent tumors

Immunology Program - *Rebecca Fuldner, Ph.D.*

Research directed toward understanding the age-related regulation of immune function in health and disease is supported by this program and includes:

- Age-related regulation of lymphocyte proliferation
- Age-related regulation of immune specificity
- Response of immune system to biochemical stimuli
- Autoimmune disease and other immunopathology related to aging
- Molecular basis of the age-related decline in immune function
- Interventions to retard and/or correct age-related decline in immune function

Musculoskeletal Biology Program - *Jill Carrington, Ph.D.*

This program supports high quality age-related basic molecular and cellular research toward development of preventative and intervention strategies to extend the health span of the elderly. Areas of investigation in this program include:

- Osteoblast and osteoclast function and bone matrix
- Muscle structure and function
- Cartilage and soft connective tissue
- Skin and wound healing
- Molecular basis of osteoporosis and osteoarthritis and
- Molecular mechanisms of the above age-related changes

Physiology Program – *Frank Bellino, Ph.D.*

Underlying age-related biologic changes that affect the function of organs and systems that impact the health of middle-aged and older people, including:

- Adrenal
- Renal
- Non-endocrine aspects of male and female reproductive tissue
- Gut, bladder

Office of Biological Resources and Resource Development

Nancy L. Nadon, Ph.D.

The NIA provides several resources developed to support research in the field of aging.

- **Aging Rodent Resources**. Because most investigators have neither the facilities nor the resources to develop and maintain colonies of aged animals in a barrier facility, the NIA provides support for both rat and mouse colonies for use by the scientific community. Available rodent resources include: four inbred strains of mice (C57BL/6, BALB/cBy, CBA, DBA/2, all from Jackson Laboratory stock), four hybrid strains of mice (B6C3F1, B6D2F1, CB6F1, 4-way cross [CB6F1 x C3D2F1]), two inbred strains of rats (F344 of NIH stock origin and Brown Norway of TNO Netherlands stock origin), one hybrid rat strain (F344BN F1), and a limited supply of calorically restricted rodents (F344, BN, F344BNF1, C57BL/6, B6D2F1, BALB/cBy).

  Information on the NIA aged rodent colonies and ordering procedures can be obtained at http://www.nih.gov/nia/research/rodent.htm. For specific information regarding availability of rodents from any of the NIA colonies, contact:

  Order Desk
  Office of Biological Resources and Resource Development, NIA
  Phone: 301-496-0181
  E-mail: obrrd_order_desk@nia.nih.gov
  E-mail inquiries also can be addressed to: rodents@nia.nih.gov

- **Aged Rodent Tissue Bank:** In late 2001, a new resource will be available from the NIA. The Aged Rodent Tissue Bank will contain flash-frozen tissue and organs from animals of limited strains and ages in the aged rodent colonies. Contact the OBRRD Order Desk for information.

- **Non-Human Primates:** The NIA supports approximately 150 rhesus macaques for aging research. Inquiries regarding the use of these animals should be directed to:

  Nancy L. Nadon, Ph.D.
  Phone: 301-496-6402
  e-mail: NadonN@nia.nih.gov

- **Aging Cell Repository:** To facilitate research on cells in culture, the NIA provides support for the NIA Aging Cell Repository located at the Coriell Institute for Medical Research in Camden, New Jersey. The purpose of this repository is to acquire, develop and characterize, store, and supply cell cultures for gerontological research. The catalog for the NIA Cell Repository is available at http://locus.umdnj.edu/nia. For additional information about the Repository, contact:

  Robert T. Johnson, Ph.D.
  Director, Aging Cell Repository
  Coriell Institute for Medical Research
  401 Haddon Avenue
  Camden, NJ 08103
  Phone: 800-752-3805

- ***C. elegans* Genetic Stock Center:** The NIA provides partial support for the *Caenorhabditis* Genetic Center located at the University of Minnesota. This stock center contains over 1,000 strains of *C. elegans.* To obtain information about this collection contact:

  Robert Herman, Ph.D.
  Caenorhabditis Genetics Center
  Department of Genetics and Cell Biology
  University of Minnesota
  St. Paul, MN 55108
  Phone: 612-624-6203

SELECTED BAP RESEARCH INITIATIVES

Caloric Restriction. Most multicellular organisms exhibit a progressive and irreversible physiologic decline during the aging process. The only intervention known to universally slow the intrinsic rate of aging in mammals is caloric restriction. Laboratory rodents and other non-primate animals given all necessary nutrients, at food intake levels of 30 to 40 percent fewer calories than *ad libitum* fed animals, live far beyond their normal life spans. These animals experience delayed onset of several diseases, especially cancers. In a recent study, the gene expression profile of the aging process was analyzed in skeletal muscle and brain of mice. Of the more than 6,000 genes surveyed, less than 1% display a greater than two-fold decrease in expression. Thus, the aging process is unlikely to be due to large, widespread alterations in gene expression. Rather, the major effect of caloric restriction seems to be to heighten animals' stress response to damage to proteins and other large molecules. This is the first global assessment of the aging process in mammals at the molecular level. Potentially, gene expression profiles can be used to assess the biological age of mammalian tissues, providing a tool to evaluate experimental interventions.

Endocrinology and Reproductive Aging. Studies are ongoing to improve our understanding of the basic biology of reproductive aging. A large body of research addresses the physiological processes and underlying molecular and cellular mechanisms of the menopausal process and their relation to the postmenopausal increase in women's health problems associated with the cardiovascular, skeletal, and genitourinary systems. Other studies vital to this area are being conducted on: 1) the steady age-related declines in testosterone observed in older males which could contribute to the decreased muscle and bone capacity observed in frail older men; and 2) the implications of human growth hormone and its effect on aging and the development of non-insulin dependent diabetes in adults.

Immunobiology of Aging. Age-related immune dysfunction is a serious problem that leads to increased morbidity and mortality in the elderly population. Thus, prevention of immunity loss would make a significant contribution to improving the health span and quality of life of older Americans. As a result of NIA's stimulation of research in this area, progress is being made in defining the mechanisms that underlie the decline of immune function that often accompanies advancing age. The success of research in this area has broad implications for vaccine development and reduction in infectious illness, which often leads to hospitalization and death in older people.

Longevity Associated Genes (LAG). NIA researchers have identified several "longevity genes" that can double or triple the life span of experimental animals. Three genes have been identified that are involved in determination of life span in the worm, *C. elegans*. These genes appear to be involved in the worm's nutrient-sensing pathway. Moreover, these *C. elegans* genes have striking homologies to genes found in mammals, including humans. The similarities between the protein produced by this particular gene (*daf-2*) and the human insulin receptor may advance understanding of how human insulin regulates metabolism and why this regulation fails in diabetes.

Mitochondrial Function and Aging. One hypothesis of the cause of aging is the accumulation of mutations in mitochondrial DNA (mtDNA). By use of a sensitive method to look at point mutations, researchers found hard evidence that mtDNA point mutations increase with aging and mitochondrial function deteriorates as people age. One particular point mutation in the control region of mtDNA replication occurs in a high proportion of the mtDNA molecules of more than 50% of people over age 65, but is absent in younger individuals. Because the mitochondria are the cellular sites for energy metabolism, deterioration of mitochondrial function may deprive cells of the energy they need to function, and ultimately could lead to premature cell death.

Muscle Aging. Loss of muscle mass and strength is a hallmark of aging and can lead to weakness, frailty and loss of independence in elderly individuals. The goal of BAP-supported research in this area is to better understand the cellular and molecular mechanisms underlying age-related changes and loss of function in skeletal muscle. Recently, researchers tested whether muscle-specific expression of IGF-I (insulin-like growth factor-I) can prevent, or as least attenuate, age-related loss of muscle mass and strength without affecting other parts of the body. To ensure that it would only be expressed in muscle, they modified the control regions of the gene. A second approach was to inject the modified IGF-I gene directly into muscle. Two important hallmarks of aging muscle were prevented by retroviral IGF-I administration. IGF-I over-expression both increased the size of existing individual muscle fibers with concomitant increases in muscle force in the aged mice, and completely prevented the age-related loss of the fastest and most powerful muscle fiber types in skeletal muscle. Importantly, because the gene was injected directly into muscle, there was no change in plasma IGF-I levels. This area of study will continue to expand. A continued improvement in understanding aging muscle biology will lead to effective intervention strategies to reverse and/or prevent age-related muscle atrophy and dysfunction in older individuals.

Telomeres and Mammalian Aging. Telomeres are highly repetitive DNA sequences located at the end of chromosomes. They are essential for the stability of chromosomes and cell survival in a wide variety of organisms. In human cells grown in culture, telomere length shortens with each cell division and progressive telomere shortening ultimately limits the ability of cells to divide. To test the possible link between telomere shortening and aging of an organism, investigators created genetically altered mice lacking telomerase, an enzyme that adds new telomeric DNA sequences to existing telomeres. In this transgenic model, telomeres are progressively shortened throughout the lifespan, providing a unique opportunity to understand the cellular consequences and aging significance of telomere shortening in the living animal. Although loss of telomeres did not elicit a full spectrum of the classical symptoms of aging, age-dependent telomere shortening was associated with shortened life span, reduced capacity to respond to physiological stress, slow wound healing, and increased incidence of spontaneous cancers. As individuals age, aged organs show a markedly diminished capacity to cope with acute and chronic stress, suggesting that maintaining proliferative potential is essential for tissue homeostasis. The telomerase-deficient mouse provides a valuable model to study the role of telomere maintenance in cellular stress responses in the aging organism.

Nathan Shock Centers of Excellence in the Basic Biology of Aging. These centers, begun in 1995, are designed to stimulate and enhance research into the basic biological processes of aging, and to facilitate the planning and coordination of research on aging activities. Additionally, the centers provide a suitable environment for fellows and junior faculty to acquire research skills and experience at institutions that have demonstrated commitment to, and expertise in, basic biology of aging research. Ultimately, research at the Centers is expected to yield breakthroughs in understanding the course of normal aging and diseases and conditions that affect older people, such as frailty and cancer. The centers are named for Nathan W. Shock, Ph.D., the first scientific director of the NIA, and a pioneer in the field of aging research.

Musculoskeletal Aging. Osteoporosis and osteoarthritis are major health problems for both women and men as they age. Changes in bone biology may lead to loss of bone mass or bone strength. Osteoarthritis is characterized by breakdown of the cartilage of the joint with resultant pain caused when the joint no longer operates smoothly due to loss of the cartilage's cushioning properties. With aging, human muscle loses both strength and endurance due to decreased average fiber diameter, shifts in fiber types and decreased mitochondrial efficiency. The resulting weakness and frailty can be a major problem leading to loss of independence in the elderly. BAP-supported studies address changes in the extracellular matrix and cells of aging cartilage, muscle and bone and how these changes may lead to disease. Cell-cell interactions, and the balance of function in various cell types in cartilage and bone are also being addressed. Other studies are looking at the presence and recruitment of progenitor cells with aging in these tissues. These studies will yield a better understanding of changes that take place with aging, and point to interventions to correct or repair harmful changes that lead to disease. Studies on the clinical and basic biology of these same tissues are supported through several other Institutes and Programs (NIA, NIAMS, NIDCR, NIDDK) at the NIH, however, the BAP portfolio focuses on changes in the biology of these tissues with aging and consequent disease.

Prostate Growth and Aging. As men get older, the incidence of benign prostatic hyperplasia (BPH) and prostate cancer increase substantially. These pathologic processes are generally preceded by prostatic growth that begins in middle-age. Whether this growth process leads directly to an increased incidence of prostate cancer with age is controversial. The underlying biology of this age-related prostate growth process and its regulation is very poorly understood. Areas of interest to the BAP include: 1) How is the growth process regulated that leads to increased prostate growth rates in middle-age? 2) What cell proliferation mechanisms are largely responsible for these growth processes and how do cell types interact during prostate growth? 3) What environmental factors or early steroid exposure during pre- and post-natal life stages affect this process in the adult? and 4) What are appropriate animal models of age-related prostate growth processes? The answers to these and other questions could shed considerable light on prostate growth processes in older men leading to health problems associated with BPH and prostate cancer.

CURRENT BAP PROGRAM ANNOUNCEMENTS

To announce high priority areas of research, the Biology of Aging Program publishes Program Announcements (PAs) in the NIH Guide to Grants and Contracts at irregular intervals. Listed below are examples of currently active PAs. These and others are available in full text on the NIA website http://www.nia.nih.gov/data/fundbrowse.asp?area_id=1.

- The Zebrafish as an Animal Model for Development and Disease Research
- Strategies for Germ-line Modification in the Rat
- Development of Zebrafish Mutagenesis and Screening Tools
- Biology of the Menopausal Process and Associated Health Conditions During and After Menopause
- Midcareer Investigator Award in Mouse Pathobiology Research
- NIA Pilot Research Grants
- NIH National Research Service Awards for Senior Fellows
- NIA Support of Scientific Meetings as Cooperative Agreements
- Planning Grants: National Programs of Excellence in Biomedical Computing
- Earth-Based Research Relevant to the Space Environment
- Aging, Oxidative Stress and Cell Death
- NIA Pilot Research Grant
- Receptors and Signaling in Bone in Health and Disease
- Mentored Quantitative Research Clinical Scientist Development Award
- Mentored Patient-Oriented Research Career Development Award
- Midcareer Investigator Award in Patient-Oriented Research
- Minority Dissertation Research Grants in Aging
- Stages of Breast Development: Normal to Metastatic Disease
- Mucosal Immunity in Pathogenesis/Prevention of Human Disease
- Co-Activators and Co-Repressors in Gene Expression
- NIA Pilot Research Grant Program
- Bone and the Hematopoietic and Immune Systems
- Mentored Quantitative Research Career Development Award
- Biology, Development, and Progression of Malignant Prostate Disease
- Opportunities in AIDS Research Grant Program: Human Immunology
- Midcareer Investigator Award in Mouse Pathobiology Research
- Basic Mechanisms of Vaccine Efficacy
- Regulation of the Immune Response
- NIA Academic Career Leadership Award
- Gene Therapy in Aging
- Basic and Clinical Research on Immune Tolerance
- Immunobiological Aspects of Hemopoietic Stem Cells
- Alcohol, Hormones, and Medical Complications
- Dehydroepiandrosterone (DHEA) and Aging: Biologic Actions and Effects of Administration

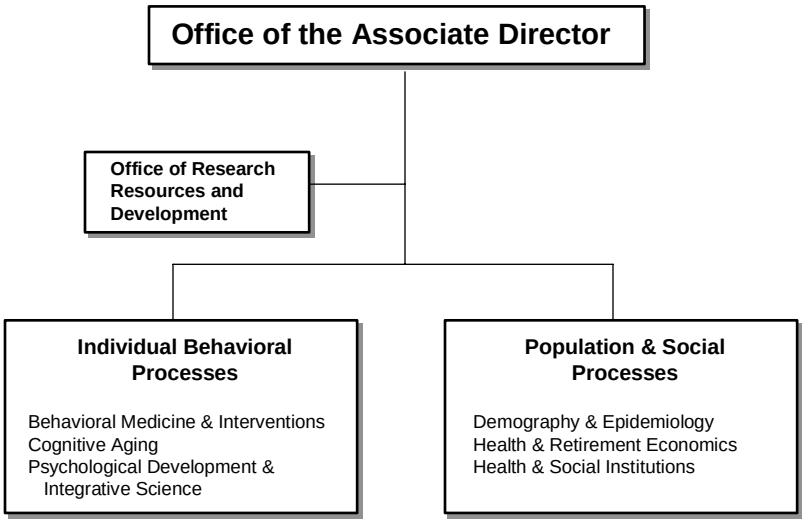
BEHAVIORAL AND SOCIAL RESEARCH PROGRAM

Richard M. Suzman, Ph.D., Associate Director
(*For further information, contact* BSRquery@nia.nih.gov)

The **Behavioral and Social Research (BSR)** program supports basic social and behavioral research and research training on the processes of aging at both the level of the individual and the society. It focuses on how people change over the adult life course, on the interrelationships between older people and social institutions, and on the societal impact of the changing age composition of the population. Emphasis is placed upon the dynamic interplay between the aging of individuals and their changing social and physical environments and on multi-level interactions among psychological, physiological, social and cultural levels. Collaboration and coordination with other NIA programs is emphasized.

The BSR program is administratively organized into two branches – Individual Behavioral Processes, and Population and Social Processes. There is substantial interaction between the two branches. A section devoted to Research Resources is housed within the Office of the Associate Director.

Behavioral and Social Research Program



DESCRIPTION OF BSR GRANT PROGRAMS

Individual Behavioral Processes - *Daniel Berch, Ph.D. and Sidney Stahl, Ph.D.* This branch supports research and training on biopsychosocial processes linking health and behavior, cognitive functioning, human factors, and integrative approaches to the study of social, psychological, and physiological influences on health and well-being over the life course. Personality and social/interpersonal relationships are investigated not only as causal variables, but also as mediators or moderators of the relationship between social/structural characteristics and health outcomes.

- **Behavioral Medicine and Interventions**. Focuses on examining the dynamic interrelationships among aging, health, and behavior processes. This unit expands traditional studies in behavioral medicine by adding an aging perspective, as well as an emphasis on the influence of the socio-cultural environment on the development and maintenance of a wide range of health and illness behaviors. This includes healthy lifestyle practices, medical self-management, and coping with chronic illnesses and disabilities. Major research topics include: 1) behavioral epidemiology; 2) disease recognition, coping and management, including physiological consequences of life stresses and burdens; and 3) social, behavioral and environmental interventions for health promotion, disease prevention, and disability postponement.

- **Cognitive Aging.** Supports research on changes in cognitive functioning over the life course. Studies are encouraged that: 1) examine the influence of contexts (behavioral, social, cultural, and technological) on the cognitive functioning and life performance of aging persons; 2) investigate the effects of age-related changes in cognition on activities of daily living, social relationships, and health status; and 3) develop strategies for improving everyday functioning through cognitive interventions. Major research topics include: higher-order cognitive processes (e.g., problem solving, decision making), social cognition, memory strategies, perceptual skills, and reading and speech comprehension. Other research is exploring the role of individual difference factors in cognitive functioning (e.g., motivation, self-efficacy, beliefs about aging, emotions, sensory limitations, experience and expertise). This unit collaborates with the NIA Neuroscience and Neuropsychology of Aging (NNA) Program to encourage research at the intersection of behavioral and neurocognition.

- **Psychological Development and Integrative Science.** Promotes research that applies an integrative approach to the study of health, behavior, and well-being over the life course. Studies are encouraged that combine diverse levels of analysis and examine reciprocal interactions among these levels. Examples include the effects of sociocultural, psychological (social, personality), biological, and genetic processes on behavioral and functional aging. In addition, research exploring factors at a single level that influence aging are welcomed.

Population and Social Processes - *Branch Chief - Rose Maria Li, M.B.A., Ph.D. and Jennifer Harris, Ph.D.* This branch supports research and training on the antecedents and impact of changing social, demographic, economic, and health characteristics of the older population. Research on the consequences of particular health care organizations and settings, as well as other social institutions upon the health, well-being, and functioning of people in the middle and later years is also supported. Comparative research is often appropriate, and interconnections with individual behavioral processes are encouraged.

- **Demography and Epidemiology**. This unit covers such topics as medical and biodemography; changes in the age structure of populations, as well as studies on the prevalence and incidence of disease and disability, and age trajectories of health; life expectancy and active life expectancy; forecasting functioning, disability, morbidity, and mortality; migration and geographic concentrations of older people; rural-urban comparisons; distributions of health services and the long-term care system; race, ethnic, and socioeconomic variations; and genetic epidemiology and population genetics.

- **Health and Retirement Economics.** This unit concentrates on the economics of aging, including but not limited to, economic and health antecedents and consequences of work and retirement; pensions and savings; health insurance and health care expenditures; Medicaid, Medicare, and Social Security; interrelationships between health and economic status, including issues related to wealth, poverty, productivity, human capital development, and economic development; the economic costs of disability; cost-effectiveness of interventions; effects of taxation policies on older people; and cross-national comparisons.

- **Health and Social Institutions.** This unit encourages research on the impact of a wide range of formal health care and related services, with particular emphasis on long-term care systems and settings and on the health and well-being of older persons. It also examines how social institutions (e.g., work, family, religion, community, living arrangements) influence health outcomes in the later years and the ways in which people influence and are influenced by the network of cultural and social institutions surrounding them.

The Office of Research Resources and Development

Richard Suzman, Ph.D. and Rose Maria Li, M.B.A., Ph.D.

The BSR Office of Research Resources and Development (ORRD) replaces the Office of Demography of Aging that was established in 1991. ORRD coordinates and implements initiatives related to research data and resources. The Office manages the Health and Retirement Study, the National Archive of Computerized Data on Aging, and all Interagency Agreements. ORRD also serves as the administrative site for the Federal Interagency Forum on Aging-Related Statistics that encourages cooperation among federal agencies responsible for the collection, analysis, development, and dissemination of data on the aging population.

BSR CENTERS PROGRAMS

Centers on Demography of Aging. Major research interests for these centers include: biodemography of aging; caregiving; costs of aging-related illness; dementia, including Alzheimer's disease; health, disability, and long-term care; health economics; intergenerational transfers and family support systems; international, comparative research; life cycle economics; linked data confidentiality; medical technologies; midlife; minority populations; morbidity and mortality risks; population and economic forecasts; socioeconomic status and health; health disparities; women; work, retirement and health; and the effect of HIV/AIDS on population age structures in Africa.

Edward R. Roybal Centers of Research on Applied Gerontology. These centers, named for retired Congressman Edward R. Roybal, former chairman of the House Select Committee on Aging, facilitate the translation of basic behavioral and social research into practical outcomes that benefit the lives of older people. The centers respond to NIA's mandate to foster research aimed at keeping people independent, active, and productive in later life. The centers are designed to move promising social and behavioral research findings out of the laboratory and into programs that can help improve the lives of older people and their families in such areas as computer skills, driving, exercise, retirement, caregiving, and nursing home care. The centers establish contacts with service providers and related industry personnel; focus on strategies to improve quality of life, enhance productivity, and minimize the need for care; and translate basic behavioral and social research theories and findings into practical outcomes.

National Archive of Computerized Data on Aging (NACDA). Operated through the University of Michigan's Inter-University Consortium for Political and Social Research (ICPSR), NACDA acquires, processes, and archives data sets concerned with the process of aging, health-related subjects, and attitudes and behavior of the aged population. Examples of NACDA's holdings include demographic, social, economic, and psychological characteristics of older adults. NACDA offers summer training courses, provides assistance to researchers using the data sets, participates in aging research meetings, and publishes a topical semi-annual Bulletin and an annual Data Collections volume. NACDA is a national resource for gerontological research into the social, demographic, economic, and behavioral aspects of aging.

Resource Centers for Minority Aging Research (RCMAR). Objectives of this program are to: increase the number of minority researchers conducting research on older populations; increase the number of researchers doing research on older minority populations; test and disseminate scientifically verifiable methods for recruiting and retaining older minority subjects in clinical, social, and behavioral research; validate and develop measurement tools useful across a variety of ethnic/racial groups; and conduct research on causes and consequences of health related disparities between minority and non-minority elders.

SELECTED BSR RESEARCH INITIATIVES

Advanced Cognitive Training for Independent and Vital Elders (ACTIVE). ACTIVE is a multisite clinical trial. This trial is unique in investigating whether common cognitive interventions can improve functioning or postpone decline using identical outcome measures. Participants are recruited with different racial, ethnic, gender, socioeconomic, and cognitive characteristics to determine the generalizability of the interventions. The 2,832 participants have been randomized into one of four groups: a group receiving memory training; a group receiving reasoning training; a group receiving speed of processing training; and a no-contact control group. After completing the training program, participants return approximately eight weeks after randomization to complete the battery of post-test instruments. Subsequent follow-ups are scheduled at yearly intervals, with booster training for half the participants after one year. NIA/NINR (National Institute of Nursing Research) staffs are actively involved in this trial as members of the Steering Committee, the mechanism for decision making and coordination.

Behavior Genetics. Rapid changes in genetics have opened up new avenues of investigation to researchers using behavioral genetic approaches, and these applications are particularly relevant to the study of aging. For example, new techniques are now available to track the developmental course of genetic contributions to behavior, identify genetic heterogeneity, and explore genetic links between the normal and abnormal. It is widely recognized that the genetic unraveling of complex traits will require a combination of methodological approaches. The recent merger of quantitative and molecular models of genetic analysis is one example of such needed strategies. In FY96 and FY97, a workshop and a symposium initiated this project. The workshop participants developed research agendas, and identified conceptual and methodological barriers to research on behavioral genetics and aging. A program announcement with set aside funds was issued in FY98 for funding in FY99 and the first training grant was awarded in behavior genetics in FY2000.

Health and Retirement Study (HRS). The Health and Retirement Study is a national panel study conducted by the University of Michigan's Institute for Social Research under a cooperative agreement with the NIA. Fully representative of the U.S. population age 50 and older, the HRS has become the nation's leading data resource on the combined health and economic circumstances of Americans as they age. The project has involved survey interviews of over 25,000 older Americans, representing the diversity of economic conditions, racial and ethnic backgrounds, health, marital histories and family compositions, occupations and employment histories, living arrangements, and other aspects of life that exist in the population as a whole. These survey participants are re-interviewed every two years (the fifth follow-up survey was completed in 2000), enabling researchers to follow the changing circumstances of the U.S. aging population and the implications of major events that take place in later life.

National Long Term Care Survey (NLTCS). The 1982, 1984, 1989, 1994, and 1999 National Long Term Care Surveys are surveys of the aged population with a particular emphasis on the aged who are functionally impaired. The samples drawn from Medicare beneficiary enrollment files are nationally representative of both community and institutional residents. The surveys provide nationally representative data on: the prevalence and patterns of functional limitations, both physical and cognitive; longitudinal and cohort patterns of change in functional limitation and mortality over 12 years; medical conditions and recent medical problems; health care services used; the kind and amount of formal and informal

services received by impaired individuals and how it is paid for; demographic and economic characteristics like age, race, sex, marital status, education, and income and assets; out-of-pocket expenditures for health care services and other sources of payment; and housing and neighborhood characteristics.

Personality in Adulthood and Old Age. Research on personality in adulthood and old age is important because personality might be linked to morbidity and mortality either directly or as a moderator variable. Some personality traits can be risk or protective health factors. For example, personality predicts awareness of current health recommendations. Autonomic response patterns such as blood pressure are functions of personality. In April 2000, BSR hosted an advisory meeting for personality and social psychology. The resulting report recommended research examining: (1) the amenability to change of personality traits related to psychological well-being and health vulnerability; (2) genetic bases, as well as physiological bases, for the relationship between personality and health; and (3) measures of personality useful for developing tailored behavioral interventions that take into account different personality profiles.

Social Psychology in Adulthood and Old Age. Research in social psychology indicates that there are age-related changes in affect regulation and expression, implicit cognition and nonconscious processes, and social cognitive processes. Research on affect and aging has implications for understanding the structure of psychological well-being and happiness across the life span, as well as suggesting possible intervention strategies aimed at maintaining the quality of life into advanced old age. Research in social cognition indicates important age-related changes in processing social information important to reasoning and decision making, to interpersonal interactions, and to social relationships. In April 2000, BSR hosted an advisory meeting for personality and social psychology. The report recommended research examining: (1) what makes people feel socially connected and how these feelings link to the immune and autonomic systems and to disease outcomes; (2) the mechanisms underlying emotional regulatory outcomes, as well as increased understanding of the neural bases of emotion and the relationship between emotion and behavior; and (3) age-related differences in how beliefs and attitudes, as well as contextual influences and individual factors, guide behavior and cognition. BSR will fund a National Academy of Sciences panel on the frontiers of social psychology.

Higher-Order Cognitive Abilities. As in earlier periods of life, older adults continue to make decisions related to everyday life, but with advanced age, new, and sometimes even more complex, decision making is required of them. Recent research indicates that age-related limitations in cognitive processing resources (e.g., executive control, speed and working memory) may impact decision making. It is generally recognized that research on higher-order processing is underdeveloped in the field of aging. In 1998, BSR drafted a program announcement entitled "Higher-Order Cognitive Functioning and Aging", and this program announcement was issued in February 2000. In early 1999, NIA asked the National Research Council (NRC) to evaluate the field of cognitive aging to identify areas of research that would improve our understanding of cognitive functioning in aging. The NRC report, entitled, *The Aging Mind*, recommended a major research initiative to understand cognitive functioning and life performance of aging individuals and to build the knowledge necessary to intervene effectively. The report identified a need for serious investigation into the ways in which older people make decisions in everyday life; particularly needed is research on decision making that requires the interpretation of new information.

Reading and Oral Language Comprehension. Late adulthood is associated with changes, generally declining, in the communicative abilities important for speech comprehension and reading comprehension. These declines can interfere with competence on instrumental activities such as: 1) taking medications and managing finances; 2) receiving accurate and appropriate medical, financial, and other types of complex information; 3) healthy social interactions, and 4) the maintenance of professional competence. The role played by differences in cognitive function between younger and older adults in comprehending written and spoken language is poorly understood. It is understood, however, that even when older adults have maintained hearing and visual acuity, they may not perform as well as younger adults on many tests of comprehension. An increased understanding of the basic processes of comprehension and the role of individual factors associated with skill acquisition, development, and maintenance will have far-reaching implications for the lives of older adults and for an aging society. NIA and NICHD (National Institute of Child Health and Human Development) published a program announcement entitled "Age-Related Changes in Reading and Oral Language Comprehension", which encourages research applications in this area.

Interpersonal Relationships in Adulthood and Old Age. Research demonstrates that social support predicts morbidity, mortality, and cognitive function in late life, above and beyond the associated instrumental assistance such support provides. In late life, there is both a reliable decrease in the amount of social contact people have and in the number of social partners they consider part of their social networks. At the same time, contacts with long-standing social partners tend to be maintained, although any number of challenges, losses, and transitions may alter the fundamental interpersonal dynamics that have characterized them over the years. All of these changes are impacted by and have important implications for basic social processes such as attribution, social comparison, emotional exchange, relationship formation, and relationship maintenance. Moreover, these changes are embedded in rich contexts in which gender, history, and culture all play major roles. Research is needed that bridges between what we know about social processes and what we know about aging and late-life development. A preliminary research agenda will emerge from an exploratory workshop held in 2000 that will form the basis for a program announcement.

Age-related Changes in Emotion and Emotional Well-being in Late Life. Current research indicates complex changes in emotion and emotional well-being in late life, changes indicative of both growth and decline. Not only are emotions important to motivation, mental health, and general well-being, researchers are finding that emotional processes are integral to cognitive processing and functioning. BSR initiated the re-issue of an expired emotion program announcement and in June 2000, along with several other institutes issued a program announcement entitled " Basic and Translational Research in Emotion." The recent NRC report, entitled *The Aging Mind*, recommended a research initiative that would increase our understanding of the role of affect in cognitive functioning and performance of aging individuals.

Alzheimer's Burdens of Care. NIA-sponsored research examines the extent, causes and consequences of the heavy burden of caring for people with Alzheimer's disease and related disorders. Current activities center on two highly visible activities: 1) the *Special Care Unit (SCU*) initiative, a set of ten collaborative projects that examines the nature and effectiveness of care in institutional settings, and 2) *Resources for Enhancing Alzheimer's Caregiver Health (REACH)*, a six-site collaborative effort to test the effectiveness of different home and

community-based interventions for helping families provide care to loved ones with mild and moderate dementia **(**see web-page at http://www.edc.gsph.pitt.edu/reach). Findings from the SCU initiative are starting to appear in the published literature (see especially the forthcoming Special Supplement on Special Care Units in "Research and Practice in Alzheimer's Disease") and research findings are being communicated to the practice community through the Workgroup on Research and Evaluation in Special Care Units (see web-page at http://www.WRESCU-NAC.org**.**)

Health-Related Behavioral Intervention Research. The links between health and lifestyle behavior (i.e., smoking, physical activity, weight and diet) are now indisputable. Understanding the determinants of health behaviors and the mechanisms linking health and behavioral processes is an essential step in designing interventions to support health promoting behaviors and to eliminate health impairing ones. During the past year, BSR health-related intervention research has focused on three related areas: 1) health practices and lifestyle factors predicting functioning, morbidity and mortality (behavioral epidemiology); 2) disease recognition and management of chronic illnesses and disabilities; and 3) the development and testing of theory based behavioral interventions. While some intervention approaches have been promising, most have had limited effectiveness in terms of intensity, duration, and/or reach of desired outcomes. More emphasis needs to be placed on intervention strategies and infrastructure needed to achieve clinically meaningful and sustainable effects for large numbers of at-risk middle-aged and older adults, as well as those with chronic illnesses or disabling conditions. BSR is developing a more integrated approach that includes multilevel interventions.

HIV/AIDS and Aging. For the past decade, NIA activities have documented the many ways in which middle-aged and older people are an integral part of the HIV/AIDS epidemic, both as victims of the disease and as caregivers. Yet, to date, scant research attention has been paid to prevention and treatment for the portion of the U.S. population over fifty. In FY1999, NIA was allocated funds by the Office of the Director, Office of AIDS Research to convene a FY2000 research agenda setting conference on Intervention Strategies for Reducing HIV/AIDS Risks in the Older Population and to update the HIV/AIDS and Aging Age-Page. Several research supplements have been awarded in 1999 and 2000 to obtain information on HIV/AIDS risks and behaviors from national data bases (e.g., HIV Costs and Services Utilization Study, Urban Men's Health Study, and Study of Women Across the Nation) and to increase our understanding of HIV/AIDS and aging issues in developing countries. In FY2000, NIA, in conjunction with the National Institute of Mental Health, entered into an interagency agreement with the Veteran's Administration to explore the feasibility of conducting the Veterans with HIV/AIDS Cohort Study (VACS).

Demography of Health. This trans-NIH initiative monitors the impact of global population aging on the burden of chronic disease and disability, identifies related health and economic trends, and researches their causes and impact. It includes initiation of new methodological approaches to generalize findings from clinical trials to the general population, especially the aged with comorbidities; continued collaboration with the World Health Organization (WHO) to improve the Global Burden of Disease modeling efforts and to enhance its ability to monitor the impact of interventions on the burden of chronic disease and disability and on the effect of global population aging; continued collaboration with WHO and the Organization for Economic Cooperation and Development (OECD) to compare economic incentives in medical care systems and relate these incentives to allocation of resources and other outcomes across population groups; promotion of research to understand disability

trends across the life course; promotion of population-based studies to provide full life-course data on health and risk factors; promotion of research to understand the impact of poor health on economic development in developing countries; improved data on burdens and costs of diseases; and addition of biologic and genetic variables to appropriate longitudinal social science surveys of the older population.

Medications and the Elderly. With chronic and multiple drug use becoming a reality, there are many opportunities for medication misuse resulting either from patient non-compliance with medical regimens or physician prescribing errors. An understanding of the interaction of age, disease, and multiple medications on clinical effectiveness and adverse drug side effects is critical. The initiative encourages research on: 1) epidemiological, social and clinical factors associated with medication use by older people; 2) social, behavioral, psychological and cognitive factors that play a role in understanding of and adherence to medication regimens; 3) the role of medical and pharmaceutical professionals in facilitating or hindering proper use of prescribed and over-the-counter medications; 4) interventions to improve medication adherence; and 5) biological factors that contribute to therapeutic outcomes in the use of medications by the elderly.

Understanding the Disability Decline and its Demographic and Economic Implications. Recent findings of reduced disability among the elderly have become prominent in the public policy debate regarding Medicare and Social Security. This initiative encourages research to: quantify contributions to the disability decline of a variety of factors, such as changing weight over time; assess international trends in disability and cross-national differences in factors that may have contributed to those health changes; develop models of supply side economic factors that contribute to and are affected by U.S. trends in disability; develop interventions to improve disability decline, based on factors found to be most important in causing the disability decline; improve projections of disease and disability rates into the future; better understand how technologies evolve in the treatment of specific chronic diseases (including generalizing from clinical trials); clarify the implications of improving health for medical care costs, including the costs of public programs, such as Medicare and Medicaid; and project the impact of the disability decline in relation to changes in family demography.

Elder Abuse and Neglect. Both the Institute of Medicine (IOM) report of a "paucity of research" on elder abuse and neglect (Violence in Families, 1998) and significant NIA supported research (Lachs MS, et al. JAMA 1998;280:428-432) demonstrate the devastating long-term consequences of elder mistreatment. Research is needed on the prevalence of elder abuse, interventions to reduce the incidence of elder abuse, and reliable measurement tools for assessing elder abuse by health care professionals.

Health Disparities. Disparities in adult health and life expectancy across socioeconomic status groups, countries, geographic areas, race and ethnic populations are well documented, however, causal mechanisms are less well understood. BSR initiatives focus on understanding the dynamics of the evolution of these disparities, and designing effective interventions to reduce them. Research, including international comparative research, is needed to understand causal mechanisms (such as intra-uterine under nutrition and early childhood growth; hygiene; advances in medical technology; health-risk behaviors; access to health care; genetic/biological factors; stress; occupational and environmental exposures) that underlie these disparities. BSR has funded an NAS Panel on Race and Ethnic Differences in the Health of Older People.

Behavioral Medicine and Biopsychology. BSR is developing a long-term research agenda at the interface between biopsychology and social structure facets, as well as psychosocial aspects of aging. Consideration is being given to integrating biology into the BSR research portfolio, increasing efforts in the areas of innovative intervention research, and encouraging methodological/statistical research on how we can best analyze the complexities of biological data. The biopsychology portfolio focuses on understanding how social/economic/behavioral influences translate into inequalities in health outcomes over time. Innovative intervention research includes a focus on primary, secondary and tertiary prevention efforts. Methodological/statistical research includes a focus on the inter-relationships among biological parameters and their relationships to other social, economic, behavioral, and other factors.

Health and Economic Development. The positive association between health and economic outcomes is widely acknowledged. However, only recently have researchers and policymakers begun to explore health status improvements as a major pathway for improving economic performance at both an individual and national level. BSR encourages continued efforts to understand health and development linkages, including better estimates of the magnitude of reciprocal effects between health and economic outcomes. Efforts include continued support for longitudinal data collection that can improve our understanding of these outcomes, and improved data quality on health status and on environmental factors that impact health.

CURRENT BSR PROGRAM ANNOUNCEMENTS

Current and active program announcements (PAs) issued by BSR are listed below and are available in full text on the NIA website at:
http://www.nia.nih.gov/data/fundbrowse.asp?area_id=2

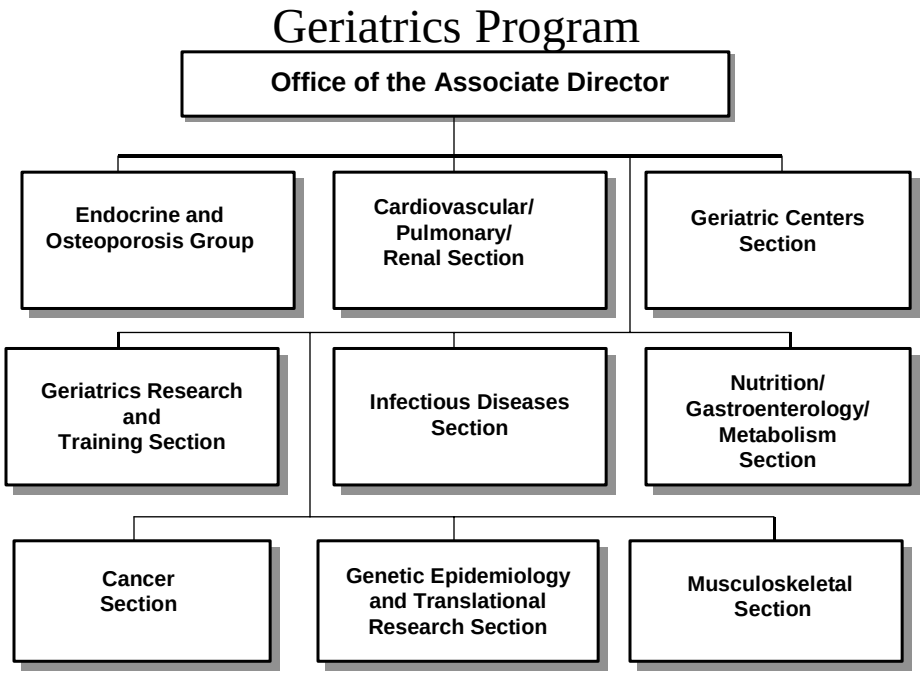
- Data Analysis and Archiving in Demography, Economics and Behavioral Research on Aging
- Age-Related Changes in Reading and Oral Language Comprehension
- Ethical, Legal, and Social Implications of Human Genetics
- Quality of Life for Individuals at the End-of-Life
- Diabetes Self-Management in Minority Populations
- Self-Management Strategies Across Chronic Diseases
- Basic and Translational Research in Emotion
- Higher-Order Cognitive Functioning and Aging
- Enhancing Adherence to Diabetes Self-Management Behaviors
- Population Movement: Determinants and Consequences
- Occupational Safety and Health Research
- Diversity in Medication Use and Outcomes in Aging Populations
- Socioeconomic Status and Health Across the Life Course
- Behavior Genetics in Adulthood and Old Age
- Health-Care Encounters Between Elderly Patients, Physicians, and Other Care Providers
- Methodology and Measurement in the Behavioral and Social Sciences
- AIDS and Aging: Behavioral Sciences Prevention Research
- Social Cognition and Aging
- Self-Care Behaviors and Aging

GERIATRICS PROGRAM

Evan C. Hadley, M.D., Associate Director

(*For further information, contact:* GPquery@nia.nih.gov)

The **Geriatrics Program (GP)** supports research and research training on the pathophysiology, diagnosis, treatment, and prevention of age-related diseases, degenerative conditions, and disabilities. A key focus is the identification of factors that slow the progression of adverse aging changes, thereby delaying or preventing age-related diseases and disabilities, and promoting healthy aging. A second important theme is the elucidation of previously unappreciated pathologies that contribute to morbidity in late life ("new" diseases of old age) and ways they might be prevented or ameliorated. A third major emphasis is on the translation of advances from biomedical aging research into new clinical applications, and testing them in controlled clinical trials.



DESCRIPTION OF GP GRANT PROGRAMS

Endocrine and Osteoporosis Group - *Sherry Sherman, Ph.D.*

- **Endocrinology.** This program area develops and supports research on age-related changes in endocrine status and function. Areas of emphasis include the physiologic processes leading to, and /or which may be sequelae of, 1) menopause in women and 2) age-related alterations in the hypothalamo-pituitary-testicular axis in men and the impact of these changes on other physiologic systems.

- **Osteoporosis.** The osteoporosis program area develops and supports basic and clinical research to identify age-associated processes that contribute to bone loss and osteoporosis; markers and risk factors that are related to decreases in bone mass, bone competence, and the predisposition to fractures; and strategies based on modifying or reversing these processes. Research on osteoporosis in advanced age is emphasized.

Cardiovascular/Pulmonary/Renal Section - *Andre Premen, Ph.D.*

- This section develops and supports a broad-based, clinically-related, extramural research portfolio on age-related changes in the cardiovascular, pulmonary, and renal systems, including the importance of these changes in age-related diseases in mature and older persons. An important focus is on age-related cardiovascular diseases and syndromes, and their prevention. Examples of research include: isolated systolic hypertension (including the importance of preventing the rise of blood pressure with age), the acute coronary syndrome, diastolic heart failure, age-related arterial wall remodeling, changes in autonomic nervous system activity, atrial fibrillation, primary prevention of atherosclerosis, and studies on age-related changes in the pulmonary and renal systems, including their impact on the aging cardiovascular system.

Geriatrics Centers Section - *Stanley Slater, M.D.*

- The Claude D. Pepper Older Americans Independence Centers (OAICs) are supported under this section. The OAICs conduct basic and clinical research to enhance the ability of older persons to maintain their independence. These centers provide support for research to develop and test interventions to prevent or delay disorders and diseases associated with aging. They also train individuals in research in these areas.

Geriatrics Research and Training Section - *Stanley Slater, M.D.*

- This section supports clinical research on disorders that are concentrated predominately among older people or that are associated with increased morbidity and mortality in the elderly. In addition, the program addresses the lack of research on clinical problems in nursing homes and other sites of long-term care for the elderly. Another mission is to attract new investigators to the field of aging and to further the development of active investigators in clinical medicine and biomedical research.

Infectious Diseases Section - S*tanley Slater, M.D.*

- This section develops and supports research on the relationship of physiologic changes associated with age or chronic disease that increase susceptibility to infections. Priorities also include new strategies to evaluate vaccine efficacy in the elderly, potential preventative techniques against infections in the elderly, and age-related changes on the effects of chemotherapy, radiotherapy, infection and other "stresses" on granulopoiesis and lymphopoiesis, and on circulating levels of amyloid proteins and effects of amyloid deposition.

Nutrition/Gastroenterology/Metabolism Section - *Chhanda Dutta, Ph.D.*

- This program area develops and supports basic and clinical research on effects of nutritional factors throughout the life span; longevity and age-associated morbidity; effects of aging on nutrient digestion, absorption, and utilization; and the contribution of nutritional status to the etiology and pathogenesis of diseases prevalent in the elderly. Chronic caloric restriction (CR) in rodents and other laboratory animals has been shown to extend life span markedly and delay the onset of numerous age-related diseases common in humans. CR also delays a wide variety of aging changes, ranging from the molecular to the organ. This phenomenon may have important implications for development of new human nutritional, endocrine, or pharmacologic disease-prevention interventions that mimic the effects of CR in experimental animals. In collaboration with NIDDK, the NIA convened an advisory group composed of basic and clinical researchers in aging, nutrition, metabolism, endocrinology, epidemiology, genetics, and other fields to consider opportunities for research on such possible interventions. The research recommendations from the Advisory Group meeting were published in a Special Issue of the *Journals of Gerontology*, "Caloric Restriction's Effects on Aging: Opportunities for Research on Human Implications." Based on the research recommendations from the Advisory Group, the GP issued an RFA, "Exploratory Studies of Sustained Caloric Restriction in Non-Obese Persons: Physiologic Effects and Comparisons/Interactions with Physical Activity."

Cancer Section - *Rosemary Yancik, Ph.D.*

- This section develops and supports research on the aging/cancer interface. Specific focus is on: age-related changes that contribute to increased cancer incidence and mortality in older persons; time, and its importance to development of cancer during a person's life span; aggressive tumor behavior in the context of the aged patient; effects of age and aging on anti-tumor drugs; and the impact of previous illnesses, disabilities, and degenerative conditions on the older cancer patient. The development of multiple primary tumors is of major interest, as is research on tumors that primarily affect older persons (e.g., breast, prostate, colon, lung, and non-Hodgkin's lymphoma).

Musculoskeletal Section - *Chhanda Dutta, Ph.D.*

- This program area develops and supports basic and clinical research on age-related changes in function of bone, muscle, and cartilage. The program supports research on geriatric rehabilitation, risk factors, prevention and treatment of falls, gait disorders and hip fractures in the elderly, and osteoarthritis.

Genetic Epidemiology and Translational Research Section – *Winifred Rossi, M.A.*

- This program area develops and supports basic and clinical research on the effects of genetic factors and gene-environmental interactions on rates of age-related physiologic and pathologic changes, differences in age of onset of diseases and disabilities, and broader outcomes not encompassed by disease diagnoses, such as exceptional longevity, in human populations.

SELECTED GP RESEARCH INITIATIVES

Claude D. Pepper Older Americans Independence Centers (OAICs). The OAICs provide support for research to develop and test clinical interventions to promote the independence of older Americans. The overall goals of the OAIC program include:

- Develop and test interventions to increase or maintain abilities needed for independence of older persons
- Strengthen core laboratories in the basic sciences as they relate to aging research
- Train researchers in the techniques of fundamental research relevant to studies in aging and geriatric medicine
- Translate OAIC research findings into improvements in health care practice through demonstration and dissemination projects.

Study of Women's Health Across the Nation (SWAN). Funded initially in September 1994, SWAN is supported by NIA (GP and BSR), the NINR, NHLBI, ORWH, NIMH, and the NCCAM. SWAN is a prospective, multi-center, multi-ethnic, multi-disciplinary study of the natural history of the menopausal transition in African-American, Caucasian, Chinese, Hispanic and Japanese women. To more fully understand the menopausal transition in socially and culturally diverse women, the specific aims of SWAN are: 1) to describe the symptoms, hormones and bleeding patterns of the menopausal transition; 2) to relate these patterns to change in markers for osteoporosis, heart disease, diabetes, and amount of fat and lean; 3) to relate personality and behaviors, including life style behaviors, to age at onset, symptoms and physical changes of the transition; 4) to consider what are menopause-related changes and what are age-related changes; and finally, 5) to describe cultural and ethnic differences among women with respect to their mid-life aging and the menopausal transition. The overall study design includes a cross-sectional study and a longitudinal cohort study using common protocols at the seven sites with clinical examination facilities.

"The SWAN Repository" was funded in 2000 at the University of Michigan. This grant supports the development of an infrastructure for the ongoing maintenance and utilization of a repository of serum, plasma, urine and DNA specimens collected from SWAN participants. Specimens will be made available to investigators from the outside extramural community,

as well as those funded directly by SWAN, in order to support the development of new proposals testing new hypotheses on menopause-related phenomena.

Use of Growth Factors and Other Agents to Prevent Physical Frailty. Administration of growth hormone to healthy older men with low naturally occurring hormone levels has been linked to increased lean body mass and decreased body fat. Additionally, several randomized, controlled studies of testosterone replacement in men over 65 years of age have resulted in increases in bone mineral density, and increases in muscle strength and lean body mass, decreases in body fat, and improved serum lipid profiles. However, results have not been consistent in all trials, and their implications for clinical outcomes are not clear, including adverse effects such as possible increased risk prostate cancer. NIA continues to conduct research to define the biologic action of these hormones and to assess the clinical utility of replacement therapy of hormones that may decline with age.

Sarcopenia. Sarcopenia is a generic term for the loss of skeletal muscle mass, quality, and strength that can lead to frailty in the elderly. Sarcopenia is believed to be due predominantly to disuse atrophy of skeletal muscle fibers. However, age-associated changes in muscle protein metabolism, nutritional status, neuromuscular function, and in the production of or tissue responsiveness to trophic factors, also may represent important underlying causes of sarcopenia. To address these issues, the NIA has convened a series of multidisciplinary workshops. The first, Workshop on Sarcopenia, was held in September 1994. The meeting proceedings and summary of the research recommendations were published in the *Journals of Gerontology*: "Sarcopenia: Muscle Atrophy in Old Age." In 1996 the workshop, "Sarcopenia and Physical Performance in Old Age," was convened to discuss research approaches to better understand the mechanisms underlying physical disabilities associated with sarcopenia. The research recommendations were published in a special issue of *Muscle & Nerve,* and a PA, "Exploratory Developmental Grants for Multidisciplinary Clinical Studies of Sarcopenia," was issued in 1997.

Role of Blood Flow in Age-Related Muscle Changes. The ability of skeletal muscle to meet its functional and metabolic demands is partly dependent on an adequate blood supply. Alterations in skeletal muscle blood flow, capillarity and/or compromised responsiveness to local and peripheral mediators of blood flow could be important pathophysiological factors of the functional and metabolic consequences of sarcopenia in the elderly. Presentations at the July 1996 NIA workshop, "Sarcopenia and Physical Performance in Old Age," indicated that improved techniques to study muscle blood supply in humans had not fully addressed age-related changes in muscle perfusion and vasculature. As a follow up of discussions during the 1996 workshop and to further explore potential consequences of aging and/or CVD on skeletal muscle perfusion, the GP held a workshop, "Changes in Skeletal Muscle Blood Supply with Aging and Disease," May 12-13, 1998. Research recommendations were published in the *Journal of Applied Physiology* in 1999. In 2000, the GP issued the PA, "Skeletal Muscle Perfusion, Aging and Cardiovascular Disease."

Cardiovascular Disease. Cardiovascular disease is the leading cause of hospitalization and death in older persons. NIA is pursuing a broad program of basic and clinical research, often in collaboration with the NHLBI. NIA research has provided important insights into age-related changes in the cardiovascular system and their relationship to age-associated disease and disability. An important focus is on preventive and therapeutic interventions designed to reduce the burden of cardiovascular disease in the elderly. Examples of current research emphasis include: isolated systolic hypertension (including the importance of preventing the

rise of blood pressure with age), the acute coronary syndrome, diastolic heart failure, age-related arterial wall remodeling, changes in autonomic nervous system activity, atrial fibrillation, primary prevention of atherosclerosis, and studies on age-related changes in the pulmonary and renal systems, including their impact on the aging cardiovascular system.

Cancer and Aging. The single greatest risk factor for cancer is aging. Close to 60% of all incident tumors and 71% of all cancer deaths occur in the age group 65 years and older. Two-thirds to three-fourths of the major tumors -- lung, colon, rectum, pancreas, prostate, urinary bladder – occur in this age segment of the U.S. population. The GP Cancer Section aims to promote development of new information on cancer in the elderly and advance the application of knowledge and techniques already developed on cancer to benefit the age group in which cancer primarily occurs. Development of this research area includes five PAs issued during 1996-2000: 1) "Aging Women and Breast Cancer," PA96-034, April 1996 (co-sponsored with NCI, NINR, and NIMH). 2) This PA was revised and re-issued as PA00-001, still entitled "Aging Women and Breast Cancer," October 1999 (co-sponsored with NCI and NINR). (3) Due for renewal is the NIA-initiated PA, "Aging, Race, and Ethnicity in Prostate Cancer," PA97-019 (co-sponsored with NCI and NIEHS). Two other NIA-initiated PAs remain current: (4) "Cancer Pharmacology & Treatment in Older Patients," PA98-069, (co-sponsored with NCI); and (5) "Aging & Age as Risk Factors for Multiple Primary Tumors," PA99-030, (co-sponsored with NIDCR). A cooperative agreement with the NCI Clinical Therapy Evaluation Program was implemented during 1999-2000 to conduct clinical trials in older-aged patients. In June 2001, the Geriatrics Program and the NCI Cancer Centers Program co-sponsored a major workshop to explore the role of the NCI-designated cancer centers to integrate aging and cancer research, and to identify scientific areas for research that could be pursued in the nation's 60 cancer centers. Research priorities and recommendations will be formulated in research areas selected by the NIA/NCI Cancer Centers Workshop Planning Committee (August 2001). These include (1) efficacy and tolerance of cancer treatment; (2) patterns of care; (3) effects of comorbidity on cancer care and treatment; (4) prevention, risk assessment, and screening; (5) patterns of care; (6) palliative care, end of life care, and pain relief; and (7) biology of aging and cancer.

Genetic Epidemiology. Genetic variation modulates risk and/or age of onset of human age-related dysfunctions, disorders and disabilities, as well as longevity and related survival outcomes. Identifying the genes responsible and their alleles' effects should lead to better strategies to prevent these conditions, increase healthy life expectancy, and evaluate individuals' risks for age-related morbidity. NIA issued an RFA: "Exploratory Projects for Longitudinal Genetic Epidemiologic Studies on Aging," in May 1999. All four NIA extramural programs developed this RFA. This RFA solicited proposals for exploratory research projects to identify appropriate populations, phenotypes, designs, and methods for longitudinal genetic epidemiologic studies to identify genetic effects on rates of age-related physiologic and pathologic changes, and/or survival outcomes such as age of onset of disease and disability. Thirty-six applications were received; eleven received NIA funding. Of the eleven funded RO1s, nine received GP funding.

CURRENT GP PROGRAM ANNOUNCEMENTS

To announce high priority areas of research the Geriatrics Program publishes Program Announcements in the NIH Guide to Grants and Contracts at irregular intervals. Active program announcements are listed below, and are available on the NIA website at http://www.nia.nih.gov/data/fundbrowse.asp?area_id=4

- NIA Pilot Research Grant Program
- Bioengineering Research Partnership
- Physical Activity and Obesity Across Chronic Diseases
- NIH National Research Service Awards for Senior Fellows
- NIA Support of Scientific Meetings as Cooperative Agreements
- Innovations in Biomedical Information Science and Technology: Phased Innovation Award
- Innovations in Biomedical Information Science and Technology: SBIR/STTR Initiative
- Skeletal Muscle Perfusion, Aging and Cardiovascular Disease
- Aging Women and Breast Cancer
- Diagnostic Imaging and Guided Therapy in Prostate Cancer: SBIR/STR Initiative
- Planning Grants for Biomedical Epidemiologic and Intervention Studies
- Mechanisms Underlying Secondary Conditions in Mobility Disorders
- Impact of Aging on Development of Atrial Fibrillation
- Aging and Old Age as Risk Factors for Multiple Primary Tumors
- Research on Tissue Engineering
- Mechanisms Underlying Individual Variations in Drug Responses
- Request for Competing Applications from the NCI Clinical Trials Cooperative Groups to Conduct Clinical Studies on Older Cancer Patients
- Genetic Architecture of Complex Phenotypes
- Cancer Pharmacology and Treatment in Older Patients
- The Impact of Immune Senescence and Maturation on Vaccine Responsiveness in the Elderly
- Exploratory Developmental Grants for Multidisciplinary Clinical Studies of Sarcopenia

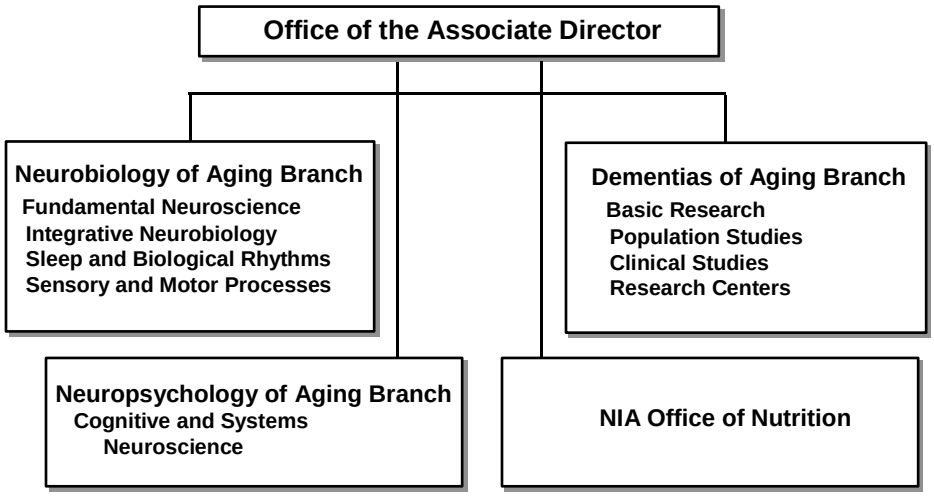
NEUROSCIENCE AND NEUROPSYCHOLOGY OF AGING PROGRAM

Marcelle Morrison-Bogorad, Ph.D., Associate Director
(For further information, contact NNAquery@nia.nih.gov)

The **Neuroscience and Neuropsychology of Aging (NNA)** program supports a broad spectrum of research and training aimed at a better understanding of age-related normal and pathological changes in the structure and function of the nervous system and how such changes affect behavior. The basic mission of the program is to expand knowledge on the aging nervous system to allow improvement in the quality of life of older individuals. This mission includes basic and clinical studies of the nervous system, clinical trials of interventions of therapeutic modalities, and epidemiologic research to identify risk factors and to establish prevalence and incidence estimates of pathologic conditions. Additionally, NNA supports research relevant to those geriatric problems arising from psychiatric and neurologic disorders associated with aging.

The National Institute on Aging (NIA) legislative mandate provides specific authority to support research on Alzheimer's disease (AD), establish the Alzheimer's Disease Patient Registry program, conduct clinical trials for the treatment of Alzheimer's disease, and promote research on the etiology, treatment, and diagnosis of Alzheimer's disease.

Neuroscience and Neuropsychology of Aging Program



DESCRIPTION OF NNA GRANT PROGRAMS

Neurobiology of Aging - *Andrew A. Monjan, Ph.D.* This branch fosters a broad spectrum of research aimed at elucidating how the nervous system is affected by normal as well as pathological aging. This research encompasses areas of neuroscience within the following categories, excluding research on the dementias of aging.

Fundamental Neuroscience - *Bradley C. Wise, Ph.D.* This section supports a wide range of research areas and methodologies under the unifying theme of research at the cellular, molecular, and genetic level that will elucidate age-related structural and functional changes. Of particular interest is selective vulnerability of neural cells to loss of function or neurodegeneration that may occur in aging. Research areas include molecular genetics of brain aging (gene and protein expression), mechanisms of neuronal cell death, mitochondrial energy metabolism and oxidative stress, protein degradation and the proteosome, glial cells in brain aging, neural stem cells and cell repair/replacement in the brain, and molecular mechanisms involved in neuronal plasticity in response to environmental influences and age.

Integrative Neurobiology - *Andrew A. Monjan, Ph.D.* This section focuses on neural mechanisms underlying age-related changes in endocrine functions; neurodegenerative diseases of aging associated with infectious agents including the epidemiology, etiology, pathogenesis, diagnosis, treatment, and prevention of neurodegenerative diseases associated with infectious agents such as HIV (AIDS dementia), herpes viruses (Herpes Zoster), and unconventional agents (prion diseases). A major focus is on the neural control of the senescence of female reproductive function, as well as the reciprocal control of the relevant hypothalamic regions by the gonadal hormones. Of growing importance is the recognition that within the intact organism, there is a network of organ systems. For example, the endocrine, immune, and nervous systems share signal molecules and transmit information within and between systems. These systems mutually regulate their complex interactions. Disruption of these interactions may result in impaired homeostatic controls leading to increased host susceptibilities to pathologic agents.

Sleep and Biological Rhythms - *Andrew A. Monjan, Ph.D.* This section encompasses the areas of study of epidemiology, etiology, pathogenesis, diagnosis, treatment, and prevention of sleep disorders of older people. Of interest to this section are studies involving: age-related mechanisms that underly circadian rhythms, sleep-wakefulness cycles and their behavioral sequelae in the aged; effects of normal and disordered circadian rhythms and other biorhythmicity upon the aging nervous system; and cellular and molecular mechanisms controlling these biological rhythms. Abnormal sleep in the older person often reflects concurrent disease states associated with profound impact on morbidity and mortality, as well as alterations of circadian rhythmicity.

Sensory and Motor Processes - *Judith A. Finkelstein, Ph.D.* This section supports research on age-related changes or impairments in sensory functions and modalities and on the cellular and molecular mechanisms underlying pathological and nonpathological sensory functioning. Areas of special research interest include elucidation of central mechanisms mediating age-associated changes or impairments in sensory functions and modalities such as hearing (presbycusis and speech discrimination), vision (acuity, depth

perception, and age-related maculopathy), vestibular system (balance, dizziness, and falls), chemical senses (olfaction and taste and their roles in appetitive behaviors), proprioception (muscle feedback), and cutaneous senses (vibratory and skin sensitivities), pain, and the cellular and molecular mechanisms underlying pathological and non-pathological sensory functioning. This section also promotes research in somatomotor processes, including molecular and cellular mechanisms of neuromotor control of striated and nonstriated muscles, disruptions of central integrative processes and/or reflex mechanisms at spinal and supraspinal levels, motor neuron diseases (e.g., ALS and postpolio syndrome), and Parkinson's Disease and Parkinsonism. Research on the effects of vestibular and other sensory-motor changes in aging, including the neural control of posture, balance and gait, and falling is also supported.

Neuropsychology of Aging - *Andrew A. Monjan, Ph.D.* This branch fosters research on interactions between the brain and behavior, endeavoring to understand how pathological occurrences, as well as normal aging processes, may affect neurologic, psychiatric, and psychological capacities. The Branch supports research from different disciplines including those of basic molecular and cellular neurobiology, experimental and physiological psychology, cognitive science, clinical neuropsychology, systems neuroscience, behavioral neurobiology, psychiatry, and neurology. The mission of the Branch is to expand understanding of the mechanisms and processes underlying cognitive, affective, and perceptual behavior over the adult life-course.

Cognitive and Systems Neuroscience - *Molly V. Wagster, Ph.D.* Research in this section emphasizes human, computational, and animal research to examine the underlying causes for the cognitive changes that occur with aging and/or experience. Studies in this area include research on attention, motivation, affect (e.g., depression and other psychiatric functions), memory, language, spatial skills, problem solving, and other higher-order cognitive capacities in normal and pathological conditions, as well as psychometric studies and clinical testing in normal aging.

Dementias of Aging - *Neil S. Buckholtz, Ph.D.* This branch fosters basic, clinical and epidemiological studies of Alzheimer's disease, cerebro-vascular disorders and stroke, multi-infarct dementias, vascular dementias, and other brain disorders of older people, including psychiatric disorders such as depression, alcohol and drug related cognitive impairment, and delirium. The Branch supports a broad range of studies of the etiology, pathophysiology, epidemiology, clinical course/natural history, diagnosis and functional assessment, drug design, drug development and clinical drug trials, and behavioral management and intervention in the dementias and other psychiatric and cognitive disorders of later life. The Branch has a major emphasis on the development of international and multinational research consortia investigations.

Basic Research - *D. Stephen Snyder, Ph.D. and Marilyn Miller, Ph.D.* Basic research in this section supports research on the etiology of Alzheimer's disease and other age-related neurodegenerative disorders, including studies to identify genetic loci associated with inherited forms of these diseases, and biochemical and molecular genetic analysis of the components of amyloid plaques, neurofibrillary tangles, and other abnormal structures found in the brains of Alzheimer's disease victims. Since it is by no means clear that plaques and tangles are the proximal causes of Alzheimer's disease neuropathology, studies are supported on all mechanisms of neuronal dystrophy and death, including the

roles of signal transduction, protein phosphorylation, proteolysis, neuroimmune function, neuroendocrine function, cerebral metabolism, toxins, trauma, and infections.

Population Studies - *Neil S. Buckholtz, Ph.D.* This section supports research in the epidemiology of Alzheimer's disease and on models for large-area registries for Alzheimer's disease and other dementing diseases of later life. Areas of special interest include domestic, cross cultural, and international epidemiological studies of the age-specific incidence and prevalence rates and risk and protective factors for Alzheimer's disease; the development and testing of models for registries for dementing diseases; familial aggregation studies; and the development of sensitive and specific cognitive and diagnostic screening instruments of use in heterogeneous and culturally varied populations.

Clinical Studies - *Neil S. Buckholtz, Ph.D.* This section supports research on the diagnosis, treatment, and management of patients with Alzheimer's disease. Research on diagnosis is aimed at the development and evaluation of reliable and valid multidimensional diagnostic procedures and instruments. Research is solicited on the identification and testing of preclinical and antemortem biological, chemical, and behavioral markers for Alzheimer's disease; on the refinement of the diagnosis of Alzheimer's disease, including studies of neuropsychological batteries, neuroimaging techniques, clinical and neuropathological concordance studies; and on the clinical course, signs, and symptoms of Alzheimer's disease.

Research in the treatment and management of Alzheimer's disease seeks to develop the knowledge base required to interrupt the course of the disease, to manage its behavioral manifestations and, ultimately, to prevent Alzheimer's disease. Treatment approaches to both the cognitive and behavioral aspects of the disease include clinical trials of pharmacologic agents and studies of behavioral and environmental interventions, individually and in combinations. Pre-clinical drug discovery, development, and animal testing studies are important aspects of this section. Research aimed at the preservation of function and reduction of excess disability, including research on wandering, insomnia, pacing, agitation, feeding and dressing difficulties, and urinary and fecal incontinence is of special interest.

Research Centers - *Creighton Phelps, Ph.D. and Elisabeth Koss, Ph.D.* This section supports the Alzheimer's Disease Research Centers (ADRC), the Alzheimer's Disease Core Centers (ADCC), and the National Alzheimer’s Coordinating Center (NACC). The ADRC program was designed to support a multifaceted approach to Alzheimer's disease, including clinical and other core services, basic and clinical research, professional and public information, and educational activities. The ADCC program provides core resources that serve as the foundation for the development of expanded multidisciplinary research activities on Alzheimer's disease. The NACC collects data from the Alzheimer’s Centers, maintains the minimum dataset and supports cooperative studies using the data.

The NIA Office of Nutrition - *Judith A. Finkelstein, Ph.D.* This office coordinates nutrition-related activities throughout the Institute and provides liaison with other agencies. The major focus is to increase awareness of the scientific community and the public of the importance of nutrition and aging research and to stimulate and encourage support of research and training in this area.

SELECTED NNA RESEARCH INITIATIVES

Alzheimer's Disease Centers (ADC). The ADCs promote research, training, and education; technology transfer; and multicenter and cooperative studies of diagnosis and treatment in Alzheimer's disease. The NIA funds 29 ADCs (17 comprehensive research centers and 12 core centers) throughout the United States. The Centers each have four cores: administrative, clinical, neuropathology, and education and information transfer. Some ADCs include other optional cores, such as neuroimaging and data analysis.

Many important landmarks in Alzheimer's disease research in this country during the last 14 years stem from resources provided by the ADCs, including the linkage and cloning of genes on chromosomes 21,14, and 1 in familial Alzheimer's disease, subsequent studies on processing of proteins coded by these genes, and the identification of the inherited risk factor, apolipoprotein E. Important clinico-pathological correlational studies relating changes of brain structure to different stages of Alzheimer's disease are being carried out in many ADCs using patients enrolled in the clinical cores, imaging supported by imaging cores and autopsy evaluation in neuropathology cores.

National Alzheimer's Coordinating Center (NACC). The NACC was established in 1999 to (a) promote data comparability among the Alzheimer's Disease Centers, (b) provide administrative information for management of the overall ADC Program, (c) index resources that are available at each Center, and (d) promote the conduct of cooperative Alzheimer's disease research. The NACC maintains a Minimum Data Set (MDS) with information about all patients and control subjects enrolled in the ADCs. It also funds cooperative research projects involving groups of Centers. As research on Alzheimer's disease has progressed, it has become increasingly apparent that, not only is Alzheimer's disease genetically heterogeneous, but also the dementias of aging are a family of diseases with a variety of overlapping phenotypes. Previously there was sparse data on heterogeneity due to the limited numbers of patients seen at any one Center. With the advent of NACC and the availability of larger data sets it will be possible to characterize the rarer and mixed phenotypes and genetic and ethnic differences that would not be possible with the smaller numbers of subjects in individual centers. It also allows research on normal aging using control subjects followed by each ADC, as well as the transition from normal aging to mild cognitive impairment to AD. By pooling patient information from many centers, it is also possible to begin to identify potential biomarkers that could help to diagnose the different variants, permit characterization of disease course, and monitor response to treatment.

Alzheimer's Disease Cooperative Study (ADCS). The major Alzheimer's disease clinical trials effort of NNA is the Alzheimer's Disease Cooperative Study. The ADCS was set up to do clinical trials on compounds which large pharmaceutical companies would generally not be interested in. This would include drugs which are off patent, or were patented and marketed for another use but might be useful for treatment of Alzheimer's disease, or novel compounds from individual investigators or from small companies without adequate resources for clinical trials. It remains the major initiative for Alzheimer's disease clinical trials in the federal government, addressing treatments for both cognitive and behavioral symptoms. This is part of NNA's effort to facilitate the discovery, development, and testing of new drugs for the treatment of Alzheimer's disease. During the first five-year grant period starting in 1991, the ADCS initiated four drug studies and two studies of assessment

instruments for Alzheimer's disease clinical trials, one in English and the other in Spanish. The results of all these have now been published or are in press. The ADCS was funded in 1996 for an additional five years. Five new trials plus an instrument study were begun during the initial four years of this grant period. These include the following: (1) phase 1 studies of AIT-082 in healthy elderly volunteers; (2) development of improved efficacy assessment measures; (3) a trial of melatonin for sleep disturbance in Alzheimer's disease; (4) vitamin E and donepezil to prevent conversion to Alzheimer's disease in patients with MCI; (5) non-steroidal anti-inflammatory drug study; and (6) divalproex sodium therapy for agitation and dementia in nursing home patients.

National Cell Bank. This genetic resource located at the Indiana University Alzheimer's Disease Center collects family histories, DNA and blood cells from patients and their families with familial Alzheimer's disease.

Brain Molecular Anatomy Project (BMAP). The BMAP is a trans-NIH initiative, broadly intended to identify and catalog the repertoire of genes expressed in the nervous system and to generate the technology and informatics systems needed to assess the cellular patterns of gene expression at various developmental stages, in aging, and in disorders of the nervous system. By constructing molecular profiles or fingerprints of brain cells, correlation of gene expression levels in defined population of cells with the clinical and pathophysiological state of the individual will provide significant new insights into the underlying mechanisms of diseases of the nervous system, yielding novel approaches to therapeutic interventions. The gene expression data resulting from the BMAP initiative will be integrated into a digital multidimensional mouse brain atlas. The interest of the NNA in this BMAP initiative is in the identification of new genes, and the regulation and cellular localization of gene expression during normal aging and in age-related diseases, such as Alzheimer's disease. During FY 2000, NNA participated in an RFA on "Gene Expression Profiling in the Nervous System" (RFA: MH-00-002), which solicited exploratory research projects using DNA microarray technology to quantify gene expression patterns in the mammalian nervous system. BMAP also made available to the scientific community a collection of greater than 20,000 cDNAs prepared from 10 brain regions, spinal cord and retina of adult mice. These cDNA and EST libraries were constructed with a BMAP supported contract to the University of Iowa, and the BMAP UniGene library is available from Research Genetics. The National Institute of Mental Health (NIMH) issued a contract (NIMH-00-DB-0006) entitled "BMAP: Gene Discovery in the Developing Nervous System" designed to discover novel genes expressed in early nervous system development and to develop a Developmental UniGene Library.

Mouse Genomics and Genetics Resources for Neuroscience. The laboratory mouse is an important organism to model complex human diseases and to understand fundamental mammalian neurobiology. Genome-wide mutagenesis is a powerful approach for the analysis of gene function, and phenotype-driven approaches are increasingly being used in mice to discover genes underlying specific behaviors. Large-scale mutagenesis efforts can generate mice with various phenotypes that can be screened for specific domains of nervous system function. Once the phenotype of interest is identified, the relevant genes and anatomical, biochemical, and physiological pathways underlying the phenotype can subsequently be elucidated. As part of the broader trans-NIH initiative on Mouse Genomics and Genetics Resources, representatives of the neuroscience-related institutes developed two initiatives that focused on mouse behavior and the nervous system. NNA participated in two RFAs, "Phenotyping the Mouse Nervous System and Behavior" (RFA: MH-99-006) and

"Mouse Mutagenesis and Phenotyping: Nervous System and Behavior" (RFA: MH-99-007), which solicited applications to develop high-throughput phenotyping assays and to establish facilities for large-scale mouse mutagenesis and phenotyping to identify genes underlying a comprehensive range of nervous system functions and complex behaviors. Identification of genes that contribute to phenotypes that undergo alterations with aging and disease are of interest to the NNA program. NNA funded two mouse phenotyping grants and cofunded three mouse mutagenesis grants.

Cognitive and Emotional Health: The Healthy Brain Project. There are now about 45 million Americans over age 60 and 117 million over age 40. Current evidence indicates that a large number of them are at substantial risk for cognitive impairment from many causes as they age. The same is true for emotional disorders. Much is known and publicized about maintaining a "healthy heart" but relatively little about the much more complex "healthy brain." While research into biological mechanisms and environmental and social effects are yielding promising results in both animal and human studies, much remains to be discovered. Through the combined efforts of three Institutes–NINDS (National Institute of Neurological Disorders and Stroke), NIA, and NIMH–the Cognitive and Emotional Health Project was launched, the goal of which is to accelerate the pace of scientific advances in the fields of cognition and emotion by development of a workshop and, ultimately, several coordinated trans-Institute initiatives. The interests of the NIA in this endeavor are central. As we age, the complex cognitive behaviors of attention, language, learning, and memory become vulnerable to insults, resulting in performance deficits that can produce frustration and concern for elders and isolate them from loved ones and society. At the same time there can be positive changes in cognitive function such as wisdom or greater integrative prowess. Advances in understanding these positive and negative changes with age, and what can be done to preserve and enhance positive outcomes, is at the core of the mission of the NIA.

Sleep Research. Studies suggest that sleep disturbances afflict a majority of the older population in the U.S. and contribute to personal discomfort and illness, caregiver burden, and overall health care costs. Sleep research encompasses age-related mechanisms that underlie sleep-wakefulness cycles and related behavioral sequelae, normal and abnormal biorhythmicity of the aging nervous system, and the effects of concurrent disease states on sleep. Research continues to develop new and more effective therapeutic methods targeted at correcting the underlying pathology of sleep disorders to replace or improve symptomatic treatment.

Improving Sensory Function. Age-associated changes in sensory function, including vision, hearing, taste, smell, proprioception, and vestibular function, can lead to significant morbidity, and decreased quality of life for many older persons. Progress is being made in discovering risk factors for age-related hearing loss and vision decline. Increased emphasis is being given to research on multiple sensory deficits in older people, which increases their risk for mortality and loss of independence. Understanding the mechanisms involved in decreased sensory function is expected to lead to interventions to maintain optimal function into the later years.

CURRENT NNA PROGRAM ANNOUNCEMENTS

To announce high priority areas of research the NNA Program publishes Program Announcements (PAs) in the NIH Guide to Grants and Contracts at irregular intervals. NNA's active program announcements are listed below and are available in full text on the NIA website at http://www.nia.nih.gov/data/fundbrowse.asp?area_id=3

- Restless Leg Syndrome and Periodic Limb Movement Disorder
- NIH National Research Service Awards for Senior Fellow
- NIA Support of Scientific Meetings as Cooperative Agreements
-
- Mechanisms in HIV Dementia and Other CNS Diseases
- Biobehavioral Research for Effective Sleep
- Curriculum Development Award in Neuroinformatics Research and Analysis
- Neuroinformatics Institutional Mentored Research Development Award
- Short Courses in Neuroinformatics
- The Human Brain Project (Neuroinformatics): Phase I & Phase II
- Relationships Among Multiple Sensory Systems
- Clinical Interventions for Managing the Symptoms of Stroke
- Xenobiotics and Cell Death/Injury in Neurodegenerative Disease
- Alzheimer's Disease Clinical Trial Planning Grant
- Alzheimer's Disease Pilot Clinical Trials
- Drug Discovery for the Treatment of Alzheimer's Disease
- Biobehavioral Pain Research
- New Directions in Pain Research
- The Zebrafish as an Animal Model for Development and Disease Research
- Neurosciences Technology Development
- Symptom Management for Chronic Neurological Conditions
- Institutional National Research Service Award in Sleep Research
- Managing the Symptoms of Cognitive Impairment

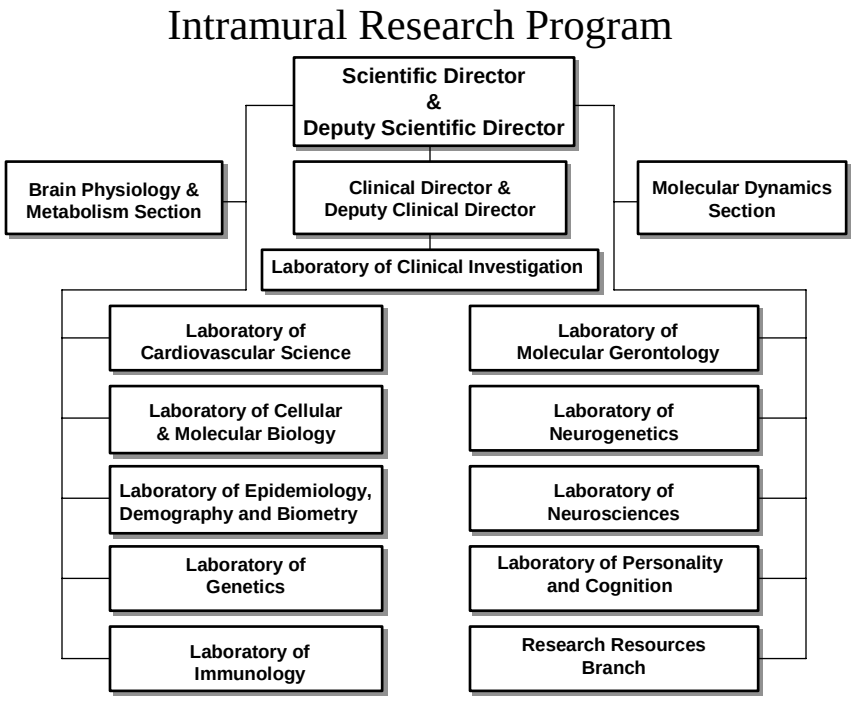
INTRAMURAL RESEARCH PROGRAM

Dan L. Longo, M.D., Scientific Director

(For further information, visit our web site: www.nih.gov/nia/research/intramural)

NIA's Intramural Research Program (IRP) includes ten scientific laboratories, two research sections, and a research resources branch. Scientific disciplines include biochemistry, cell and molecular biology, structural biology, genetics, behavioral sciences, epidemiology, statistics; medical disciplines include neurobiology, immunology, endocrinology, cardiology, rheumatology, hematology, oncology, and gerontology. Medical problems associated with aging are pursued in-depth using the tools of modern laboratory as well as clinical research. The central focus is to understand age-related changes in physiology and the ability to adapt to environmental stress. This understanding is then applied toward gaining insight into the pathophysiology of age-related diseases. Thus, common age-related diseases are under study (e.g., Alzheimer's disease, atherosclerosis, osteoarthritis, diabetes, cancer), while determinants of healthy aging are being defined.

Most IRP research is conducted at the Gerontology Research Center (GRC) in Baltimore, Maryland. The Cerebral Physiology and Metabolism Section is located in the Clinical Center on the NIH main campus in Bethesda, MD. The Laboratories of Epidemiology, Demography, and Biometry and Neurogenetics are also in Bethesda. The IRP provides a stimulating, academic setting for a comprehensive effort to understand aging through a multidisciplinary effort of investigator-initiated research. The program offers many excellent training opportunities in both laboratory and clinical medicine with a wealth of valuable resources. The NIA is committed to training researchers for lifetime careers in the biomedical and behavioral sciences.



IRP LABORATORIES, SECTIONS, AND BRANCHES

Laboratory of Cardiovascular Science
Edward Lakatta, M.D. Chief

The **Laboratory of Cardiovascular Science (LCS)**, established in 1985, is organized into two sections: **Cardiac Function and Behavioral Hypertension**. The overall goals of this Laboratory are to 1) identify age-associated changes that occur within the cardiovascular system and to determine the mechanisms for these changes; 2) study myocardial structure and function and to determine how age interacts with chronic disease states to alter function; 3) study basic mechanisms in excitation-contraction coupling and how these are modulated by surface receptor signaling pathways in cardiac muscle; 4) determine the chemical nature and sequence of intermediate reactions controlling the movement of ions through ionic channels and pumps present in myocardium, and how these are affected by aging and disease; 5) determine mechanisms that govern neuro-hormonal behavioral aspects of hypertension; 6) determine mechanisms of normal and abnormal function of vascular smooth muscle and endothelial cells; and 7) establish the potentials and limitations of new therapeutic approaches such as gene transfer techniques. In meeting these objectives, studies are performed in human volunteers, intact animals, isolated heart and vascular tissues, isolated cardiac and vascular cells, and subcellular organelles.

Laboratory of Cellular and Molecular Biology
Nikki J. Holbrook, Ph.D., Chief

The **Laboratory of Cellular and Molecular Biology (LCMB)** is comprised of seven independent research programs headed by either a tenure track scientist or a senior investigator. These programs include the Cell Stress and Aging Section, the T-Lymphocyte Signaling Unit, the Stress Signaling Unit, the Cell Cycle Control Unit, the Cancer Molecular Genetics Unit, the Molecular Neurobiology Unit and the DNA Repair Unit. Major areas of emphasis common to the individual programs include: 1) the elucidation of signal transduction processes and gene regulatory mechanisms involved in mediating cellular responses to environmental signals such as growth factors, cytokines, and stress stimuli; 2) the determination of molecular mechanisms contributing to the maintenance of cellular homeostasis and cell cycle control; and 3) the contribution of dysregulated gene expression, or loss of critical gene functions to the development of cancer. A wide variety of *in vitro* and *in vivo* models are being employed to approach these issues. These processes have direct relevance to our understanding of critical events associated with various age-related deficits and/or development of age-related diseases including cancer and Alzheimer's disease. The ultimate goal of the laboratory is to uncover knowledge that can be applied to prevent or delay the onset of age-related disabilities and disease processes, and/or provide new strategies for their diagnosis or treatment. Combined, the programs within the LCMB provide extensive and broad expertise in the areas of biochemistry, cellular and molecular biology and genetics. Specialized expertise in a variety of approaches used to analyze or manipulate gene expression is also available within the LCMB.

Laboratory of Clinical Investigation
Darrell R. Abernethy, M.D., Ph.D., Chief

The **Laboratory of Clinical Investigation (LCI)** chiefly focuses on clinical research issues of importance in gerontology. Clinical work includes the activity with volunteers on the **Baltimore Longitudinal Study of Aging (BLSA)**, the **Healthy Aging in National Diverse Longitudinal Samples Study (HANDLS)** and cross-sectional studies in a variety of age-related disease areas including diabetes, metabolism, cardiovascular disease, neurologic disease, and cancer. Diabetes mellitus is one of the most prevalent diseases among the elderly, with approximately 40% of those over the age of 65 having either diabetes or elevated fasting blood glucose levels. The **Diabetes Section** focuses on improving present methods for treating type 2 diabetic patients. Because it is most likely that it is the elevated blood sugar levels that lead to the complications of diabetes, our endeavors are directed towards improving insulin secretion or restoring insulin action. The **Endocrinology Section** conducts and facilitates (by collaboration with other intramural and extramural entities) research on the relationships of hormone secretion to nutrition and health, and the interrelationships among various hormone axes, including the growth hormone and reproductive hormone axes, during aging. Researchers are investigating the clinical utility and risk/benefit ratios of selected hormone replacement regimens designed to reverse age-related alterations of hormone balance. The **Hematology/Oncology Section** seeks to develop novel anti-tumor therapies and evaluate these and conventional therapies in an aging population. Studies are planned to explore DNA repair and other potential predictive factors in treatment of lymphoma and breast cancer. Future studies are planned to discover if "mini-transplant" approaches, i.e., immune reconstitution can be accelerated in diseases such as chronic lymphocytic leukemia. The **Longitudinal Studies Section** mission centers on the operational management of two longitudinal studies housed there. The **BLSA** is a multidisciplinary longitudinal study of human aging. The second is to perform research with the BLSA using both existing data and data from newly initiated projects. This Section performs research with the BLSA cohort using both existing data and data from newly initiated projects. The **HANDLS** is a new longitudinal study of minority health with special emphasis on age related health disparities and the influence of socioeconomic status and race on health. The **Metabolism Section** has played a critical role in evaluating diagnostic standards and in determining whether an adjustment for age is appropriate. The BLSA and the Follow-up Study of the NHANES-I have provided unparalleled data sources for this effort. The **Molecular and Clinical Pharmacology Section** studies the impact of age- and disease-related changes in calcium signaling in vascular smooth muscle on vascular responses in aging, hypertension, and atherosclerosis, and seeks to understand how such changes affect drug responses. The high prevalence of hypertension and atherosclerotic disease in the elderly makes understanding therapeutic responses and development of new therapies a priority. The **Nuclear Magnetic Resonance Unit** performs biophysical and physiological studies on human subjects, experimental animals, and tissue and cellular preparations. Current research includes imaging studies of engineered cartilage tissue, tissue biomechanics, and tissue biochemistry. The response of engineered cartilage to a variety of growth conditions and pharmacologic interventions may be assessed in detail using our methods.

Laboratory of Epidemiology, Demography, and Biometry
Richard J. Havlik, M.D., M.P.H., Chief

The **Laboratory of Epidemiology, Demography, and Biometry (LEDB)** conducts research on aging and age-associated diseases and conditions using population-based epidemiologic and biometric methods. Laboratory staff work collaboratively both within and among four sections: the **Epidemiology and Demography Section,** the **Neuroepidemiology Section,** the **Geriatric Epidemiology Section,** and the **Biometry Section** and with other NIA and outside investigators. The mission of LEDB is to elucidate the etiology of diseases of old age by combining epidemiologic data with information from other disciplines; evaluate the consistency of epidemiologic data with etiologic hypotheses developed either clinically or experimentally; and provide the basis for developing and evaluating preventive procedures and public health practices. These general principles have guided a research agenda that emphasizes three important and interrelated areas: Physical Function and Disability, Cognitive Function and Dementia, and Age-associated Diseases and Conditions – including successful or effective aging. In each area, studies are influenced by results of analytic efforts of current LEDB-sponsored studies and by opportunities created by advances in biology.

The **Epidemiology and Demography Section** plans and conducts studies on chronic diseases, functional status and disability in the older population. The **Neuroepidemiology Section** conducts interdisciplinary research on the association of genetic, molecular, and behavioral factors in relation to brain disease in old age. The **Geriatric Epidemiology Section** carries out interdisciplinary studies of the association of molecular and genetic markers with weight-related health outcomes including cardiovascular risk factors and disease, and musculoskeletal diseases. The **Biometry Section** conducts research in the mathematical, statistical and numerical aspects of aging and health. This Section provides statistical consulting, computing, graphics, and data management services to the other units within LEDB. Senior LEDB staff consult with other components within the IRP, NIA, other NIH Institutes, other Government agencies, and the private sector. LEDB research interests use data from the Established Populations for Epidemiologic Studies of the Elderly (EPESE), the Women's Health and Aging Study (WHAS), the Honolulu-Asia Aging Study (HAAS), the Health and Body Composition (Health ABC) Study, the Veterans' Study of Memory in Aging, the MacArthur Studies of Successful Aging, and other epidemiologic studies.

Laboratory of Genetics
David Schlessinger, Ph.D., Chief

The **Laboratory of Genetics (LG)** was established in 1997, with a **Human Genetics Unit, a Transcription Remodeling and Regulation Unit, a Gene Recovery and Analysis Unit,** and **a Developmental Genomics Section**. The interests of the Laboratory are based on the view that aging has genetic determinants as an integrated part of human development, with a profound dependence on the interplay of synthetic and degradative processes that are initiated *in utero*. Five major types of study are in progress: 1) Transitions between immortal and mortal cells, particularly at the level of large-scale regulatory phenomena at the level of chromatin. The transition of immortal embryonic stem cells to mortal differentiating cells is a fundamental feature of the initiation of aging in metazoans. The genes specifically activated and repressed during such transitions are being studied in mice and in developing embryonic stem cells (in the Developmental Genomics and Aging Section.) 2) Cohorts of genes involved in the development of selected "nonrenewable" systems. To understand and

ultimately try to compensate for loss of cells and tissues during aging, skin appendage development is being studied. Studies start from human or mouse hereditary defects that have been attributed to single genes, such as the ectodysplasin-A involved in X-linked ectodermal dysplasia. 3) Nuclear organelles that determine large-scale chromatin remodeling events. Such events are involved in chromosome dynamics related to large-scale control of gene expression. A combination of approaches is being used to isolate and characterize critical complexes, including the one that is modified to cause the Werner premature aging syndrome. 4) Genes involved in embryonic events that prefigure aging-related phenomena. The Human Genetics Unit is studying overgrowth syndromes, in which the set point of size of tissues and organs is determined in fetal life; and premature ovarian failure, in which the aging phenomenon of early menopause is determined by an increased rate of follicular atresia during fetal life. 5) The genetics of aging-related complex conditions is being approached by interactive studies of the "founder" population in Sardinia. Initial phenotypes to be studied along with epidemiological factors include arterial stiffness and selected psychiatric/ psychological traits.

Laboratory of Immunology
Dennis D. Taub, Ph.D., Acting Chief

The interests of the **Laboratory of Immunology (LI)** cover a wide range of topics devoted to a greater understanding of the biological, biochemical, and molecular alterations in immune functions that occur within individuals during both normal and disease-associated aging processes. A common goal of these research programs is the elucidation of the age-related deficits in immune function that could be potentially targeted by various therapeutic strategies. Areas being studied include: 1) a role for various cytokines, hormones, and chemokines in leukocyte trafficking, cellular activation, and apoptosis; 2) the biological and molecular mechanism of HIV-1 entry and propagation in Th/Tc subsets and mononuclear cells obtained from young and elderly individuals; 3) the preclinical and clinical development of immunologically-based protocols especially those focused on promoting cellular responses in elderly populations with the ultimate goal of improving the immune function of aged and cancer-bearing individuals; 4) the molecular examination of telomere length, telomerase activity, and the various factors and genes that appear to be differentially regulated during human lymphocyte development, differentiation, and activation; 5) identification and characterization of immunosuppressive factors associated with cancer-based immunosuppression; 6) defining various oncogenes and signaling/cytoskeletal components involved in various signaling pathways within lymphocytes; 7) the development of protein-conjugate vaccines for *Streptococcus pneumoniae* for use in various immunoglobulin transgenic and knockout animal models, as well as in the highly susceptible elderly populations; and 8) the process of generating the development of the B-cell repertoire for antigen responses.

Laboratory of Molecular Gerontology
Vilhelm A. Bohr, M.D., Ph.D. Chief

The **Laboratory of Molecular Gerontology (LMG)** investigates DNA-related mechanisms such as genomic instability, DNA repair, DNA replication, and transcription. We consider the increased DNA damage accumulation in senescence to be the major molecular change with aging. This DNA damage may eventually inactivate individual genes. Inactive genes lead to deterioration of the organism; this deterioration is characteristic of the senescent phenotype. DNA damage also may be a major cause of age-associated diseases, notably cancer. One goal of the LMG is to understand the underlying mechanisms involved in DNA damage formation, the changes that take place with aging, and the factors that make aging cells susceptible to cancer. The LMG has a special interest in the fine structure of DNA repair, including the DNA repair process in individual genes. Scientists are investigating the molecular mechanisms involved in DNA repair and in genomic instability in normal, senescent, and cancer cells. Other researchers are investigating nucleotide excision repair and base excision repair *in vitr*o, in fractionated cell extracts, and in intact cells. The Laboratory also is interested in the molecular processes that interact with DNA repair. These include transcription, replication, somatic mutation and mitochondrial alterations.

Laboratory of Neurogenetics
John Hardy, Ph.D.

This new laboratory, opening in July 2001, has the potential to develop an understanding of the major neurodegenerative diseases using genetic approaches. This laboratory will collect families with familial Alzheimer's disease, Parkinson's disease and other related conditions and try to identify the genetic lesions that cause the disease. Once investigators have identified the genetic lesions, they will attempt to develop an understanding of the disease process by examining the function of the normal protein and determining how the function of the mutant protein is different, both in cells and in transgenic mice. They have been extremely successful, and have identified mutations that lead to Alzheimer's disease and Pick’s disease. This laboratory will be working to identify two genes they have found that contribute to Parkinson's disease, as well as genetic risk factor loci for late-onset Alzheimer's disease.

Laboratory of Neurosciences
Mark P. Mattson, Ph.D., Chief

The aging process in the nervous system shares many mechanisms with the aging process in other organ systems. At the biochemical and molecular levels, such age-related changes include: increased oxidative damage to proteins, DNA, and lipids; perturbations of energy metabolism; and alterations in the regulation of cell proliferation and death. At the functional level, both speed and accuracy of a range of behaviors, including cognition and control of body movements, are impaired. Due to improved preventative and therapeutic measures for cardiovascular disease and cancers, the average age of our population continues to increase. Unfortunately, accompanying the increase in life span there has been a progressive increase in the numbers of persons with age-related neurodegenerative conditions such as Alzheimer’s disease, Parkinson’s disease, Huntington’s disease, amyotrophic lateral sclerosis and stroke.

Two major goals of research in the **Laboratory of Neurosciences (LNS)** are to understand normal aging of the nervous system at the cellular and molecular levels, and to identify the mechanisms responsible for age-related neurodegenerative disorders. Knowledge gained in such basic research is then used in preclinical studies to develop interventions such as changes in diet and lifestyle, and development of drugs and cell therapy techniques to prevent and treat these disorders. Studies are being conducts by LNS scientists in: Oxidative Stress and Calcium Regulation; Apoptotic and Neuroprotective Signaling Pathways; Synaptic Signaling and Plasticity; Stem Cell Biology; Telomerase; Invertebrate Genetics; Inflammatory Processes; Behavior; and Diet and Lifestyle.

Laboratory of Personality and Cognition
Paul Costa, Jr., Ph.D., Chief

The fundamental scientific paradigm guiding research in the **Laboratory of Personality and Cognition (LPC)** is the analysis of individual differences. Few phenomena are more basic than the fact that human beings differ—in health, in rates of aging, in cognitive ability, in personality, in happiness, and in life satisfaction. The LPC 1) conducts basic and clinical research on individual differences in cognitive and personality processes and traits; 2) investigates the influence of age on these variables and their reciprocal influence on health, well-being and adaptation; and 3) employs longitudinal, experimental, and epidemiological methods in the analysis of psychological and psychosocial issues of aging, including health and illness, predictors of intellectual competence and decline, models of adult personality, and correlates of disease risk factors. **The Personality, Stress, and Coping Section** conducts basic and applied research on personality as it relates to aging individuals including studies of stress and coping, mental and physical health risks and outcomes, adaptation and well-being. Basic research centers on a taxonomic model of personality traits and its assessment. **The Cognition Section** conducts studies that attempt to distinguish pathological from healthy, age-related cognitive changes in a broad range of cognitive tasks including short-term and long-term memory, visuo-spatial rotation, attention, and decision tasks. In addition, structural and functional brain changes are examined using MRI and PET. Studies are performed on regional structural brain changes, especially the hippocampus, and their relationship to cognitive performance and dementia. Regional differences in cerebral blood flow derived from PET studies at rest and during cognitive challenge are related to aging and patterns of cognitive change.

Brain Physiology & Metabolism Section
Stanley I. Rapoport, M.D.

The **Brain Physiology and Metabolism Section (BPMS)** studies brain phospholipid metabolism in intact animals and humans, as well as synaptic integrity and function in aging and Alzheimer's disease (AD). Methods involve *in vivo* tracer studies, chemical analytical techniques quantitative autoradiography, and PET. Studies are related to neuroplasticity and signal transduction, central action of drugs, and nutritional regulation of brain fatty acid metabolism. Brain incorporation from plasma of labeled arachidonic acid is increased in response to cholinergic and dopaminergic agonists in rat models of AD and Parkinson disease reflecting upregulation of phospholipase A_2 mediated signal transduction. Upregulated signaling may be imaged in the human brain using PET and [C^{11}] arachidonic, and may help to elucidate disease mechanisms and provide early diagnosis of

neurodegenerative disorders. *In vivo* imaging methods using PET were developed to examine brain blood flow and metabolism in patients with AD and in healthy control subjects. The activation, or stress paradigm, was shown to quantify synaptic integrity, which declines with dementia progression in AD in two stages - the first potentially reversible and sensitive to synaptic enhancing drugs (e.g. physostigmine), the second irreversible and associated with mitochondrial and synaptic dropout.

Molecular Dynamics Section
Joseph M. Rifkind, Ph.D.

The **Molecular Dynamics Section** focuses on the interplay between structure and dynamics and how these influence biological function. The section presently is involved in studying the structural and dynamic factors in hemoglobin that regulate the binding of oxygen, as well as autoxidation with its associated release of superoxide. The finding that autoxidation of hemoglobin is appreciably enhanced at reduced oxygen pressures has lead to the proposal of a novel method for producing oxyradicals under hypoxic conditions. Studies are being performed on erythrocytes, interaction of erythrocytes with other tissues and with laboratory animals to determine to what extent this mechanism contributes to the pathophysiology of aging.

Research Resources Branch
Alan B. Zonderman, Ph.D., Chief

The **Research Resources Branch** provides centralized research resources and research support services essential to the productive conduct of biomedical research by the Intramural Research Program. The Branch is divided into eight sections that focus on particular specialties or types of service: Central Laboratory Services, Comparative Medicine, Data Management Services, Instrumentation, Design and Fabrication, Library and Information Services, Network, Computing and Telephony, Photography and Arts, and Statistical and Experimental Design. Central Laboratory Services is subdivided into the Clinical Core Laboratory, Confocal Microscopy, DNA Array Facility, Flow Cytometry, Genotype Services, and Mass Spectrometry. The Comparative Medicine Section includes animal husbandry for a variety of species, producing transgenic and knockout rodents, and the breeding, weaning, and mating of rodents consistent with the genetic model from which they derived.

SELECTED TRANS-NIA ACTIVITIES AND NIA RESEARCH COLLABORATION

Description

To assist in administering the broad scope of aging research, NIA staff participate in various collaborative activities both within the Institute and with other organizations. Collaboration within NIA often is facilitated by Working Groups, which include:

Aging and Cancer	Clinical Trials
AIDS and Aging	Endocrinology/Menopause
Alzheimer's Disease	Genetic Basis of Aging
Cardiovascular Aging	Minority Aging

There also are NIA offices that coordinate Institute research activities, including the NIA Office of Nutrition (based in the Neuroscience and Neuropsychology of Aging program), and the Office of Research Resources and Development (based in the Behavioral and Social Research program.) In other areas, such as women's health, disease prevention, and international activities, a specific staff member has been designated as coordinator.

This section describes trans-NIA activities on minority aging and women's health, and summarizes NIA's collaborative research activities with other NIH institutes and other federal agencies.

Minority Aging

J. Taylor Harden, Ph.D.
Assistant to the Director for Special Populations

The health status of all U.S. racial and ethnic groups has improved steadily over the last century. However, disparities in major health indicators among segments of the U.S. population, white and non-white groups, are growing. In general, African American, American Indian, and Hispanic ethnic and racial groups are disadvantaged relative to whites on most health indices, whereas Asian Americans appear to be as healthy, if not healthier, than whites on most indicators. A key component of the Institute's mission is to better understand age-related diseases and problems of older persons - this mission involves a special focus on U.S. minority population elders.

For over a hundred years, medical and social scientists have studied differences in health status among racial groups in the U.S. However, in the last twenty years, scientific inquiry has moved from simple descriptions of health differences between racial groups to attempts to explain the underlying factors that account for the differences. According to Kington and Smith (1997) understanding these underlying causes requires disentangling a complex mesh of factors labeled as age, race, socioeconomic status and health.

NIA's minority aging activities are conducted by each of the NIA Programs. These activities include basic science studies, clinical and epidemiologic research on the health and

well-being of minority elders, demographic studies on the growth of minority populations, social aspects of aging, and efforts to recruit minority individuals into clinical studies on minority aging. Other NIA initiatives are designed to increase the number of minority investigators involved in aging research. A set of recommendations, outlined below, was developed by a recent ad hoc panel that reviewed NIA's minority aging research and training portfolio. The recommendations in addition to the NIA's Strategic Plan to Address Health Disparities have the potential to significantly influence NIA program priorities, NIA planning processes, and ultimately the health of America's rapidly growing minority-aging populations.

The Minority Aging Research Review Committee, in partnership with the National Advisory Council on Aging, engaged in a yearlong process that included meetings, review of substantial background material, conference calls, and electronic communication. Eight recommendations were developed for action by the NIA that should improve understanding of how to improve the health status of minority elders and expand participation by under-represented scientists in aging research. The recommendations build upon the combined experience of the review panel representing decades of accumulated knowledge and experience. The recommendations are diverse but not mutually exclusive.

Recommendations

Eliminate health disparities: Disentangle socioeconomic status (SES), environmental exposure, and race and ethnicity status on health. Improve knowledge regarding prevalence of, and risk factors for, Alzheimer's disease, dementia, and other neurological and psychological disorders. Conduct a review of the Alzheimer's Centers and Satellite programs to determine participation and research relevance for minority populations. Conduct research on the impact of SES, environmental exposure, health behaviors, race and ethnicity on differences in disease prevalence (cancer and cardiovascular disease), incidence, morbidity, and mortality among older population groups.

Define race, culture, ethnicity, and SES: Continue to work toward clarifying the most appropriate definitions of, and use for, the concepts of race, culture, and ethnicity in aging research. Improve the working definitions of race, ethnicity, culture, and SES and encourage standardization across studies. Host a conference to initiate a discussion of measuring and explaining cross-racial/cross-cultural differences in health and disease outcomes among various subpopulations. Examine the contribution of the IRP's Baltimore Longitudinal Study of Aging (BLSA) as a means to improve understanding of race and socioeconomic effect on health and effect of health on SES.

Implement longitudinal and life course studies: Longitudinal, population-bases studies are encouraged to improve understanding of differences in life experience, exposure to risk factors, use of health services and health outcomes among various populations.

Integrate biology, genomics, and genetics of aging: Genetics research is encouraged but with caution and sensitivity. Continue research on biological and genetic variations that address the relationships among genetic variations and social and cultural conditions within and among ethnic and racial minority groups. Support the BLSA in clarifying and extending genetics research to focus on health issues and successful aging across population groups.

Refine methods and strategies: Support research to improve methods and strategies for conducting research with minority populations. Improve instruments and methods, including standardization across populations, to study cognitive disorders and mental health decline in minority populations. Improve scales and instruments for use across older population groups.

Iimprove recruitment and retention of minorities in research: Encourage NIA to support research to improve strategies for recruitment and retention of minority elders in research with goals of hypothesis testing; assist the NIH to clarify the process of monitoring the inclusion of minorities in clinical studies.

Strengthen and clarify the NIH policy on inclusion of minorities in clinical research: Seek to improve the NIH implementation of the policy on inclusion of women and minorities in clinical research. Encourage the NIH and the NIH/Office of Research on Women's Health (ORWH) to design a system for tracking inclusion of women and minorities in clinical research that will allow program staff to review recruitment and retention data as well as data that track the performance of investigators in meeting the mandate and intent of public law.

Build capacity and enhance training and information dissemination: Devote resources to facilitating networks of scholars focusing on minority issues and to conferences focusing on common issues in career development; encourage NIA to commit to long-term support of the Resource Centers for Minority Aging Research (RCMARs); continue to support, develop and expand existing mechanisms for developing scientists focused on topics relevant to the aging of minority subpopulations; support mentoring of new investigators; expand physician scientists opportunities; disseminate information.

Conclusions

This review of minority programs at the NIA was prompted by the coming demographic revolution in the numbers of older minorities, as well as a concern with finding the most effective and efficient use of limited resources in the future. Across most of the program areas of NIA, there is active research on issues relevant to minority aging. While none of these is of a sufficient size and scope to answer the multitude of questions relevant to all of minority health, ongoing and special initiatives are directed toward these issues and NIA continues its efforts to develop innovative programs and strategies.

Women's Health

J. Taylor Harden, Ph.D.
Assistant to the Director for Special Populations

Women make up a majority of the older population comprising 58 percent of the population age 65 and older; by 85 and older, women comprise 70 percent of the population. Older women are less likely than older men to be married and are more likely to live alone. In 1998, about 41 percent of women over age 65 were living alone, compared with 17 percent of older men. The combined factors of men generally being older than their spouses and higher life expectancy for women contribute to the proportion of women living alone, the earlier institutionalization of women than men, and disproportionately high level of poverty (Bureau of the Census, 1996, 65+ in the United States). The death of a husband often marks the point of acute economic reversals for the surviving wife.

The NIA supports a diverse portfolio of research on older women's health addressing health and wellness, neuroscience and neuropsychology of aging, basic biology of aging, diseases and conditions of older adults, and behavioral and social problems of older women. NIA research includes several long-term research areas that focus on health issues of older women including dementia and Alzheimer's disease, menopause and hormone therapy, osteoporosis and age-related muscle loss, physical disability, caregiver burden, decline in function of older women, hip fractures, and cancer in older aged women. Described below is a selection of four significant and long-term research grants at the NIA: Prevention of Cognitive Decline in Women, Study of Women's Health Across the Nation (SWAN), Study of Osteoporotic Fractures (SOF), and a study on Osteoarthritis.

Prevention of Cognitive Decline in Women. In the United States, 5 percent of women over age 60, and 28 percent over 85 likely have some form of dementia. NIA investigators are capitalizing on a large epidemiologic dataset with 22 years of prospective data to study risk factors for early cognitive impairment. While advances have been made to delay Alzheimer's disease progression, little research is aimed at studying the earliest stages of cognitive decline in healthy women, which might be most susceptible to intervention. Prior investigations have been largely cross-sectional, and smaller than the proposed study; virtually no studies have explored interactions between environment and genetic factors. The investigators of this study are examining prospectively how estrogen use, antioxidant intake, and anti-inflammatory drugs influence cognitive decline in non-demented women; they will examine the duration and dose of these agents, and explore interactions with genetic factors. The investigation is being conducted within the Nurses' Health Study, a cohort begun in 1976 with 121,700 women. The Nurses' Health Study provides a highly cost-efficient setting to examine lifestyle and genetic influences that may be instrumental in preventing or delaying early decline in cognitive function.

Study of Women's Health Across the Nation (SWAN). SWAN is supported by the NIA, the National Institute of Nursing Research (NINR), the National Heart, Lung and Blood Institute (NHLBI), the National Institute of Mental Health (NIMH), the National Center for Complementary and Alternative Medicine (NCCAM), and the NIH Office of Research on Women's Health (ORWH). Currently 1.3 million U.S. women become menopausal each year, and this number is steadily increasing. As they reach this landmark, women and their doctors continue to seek accurate information about subsequent health in terms of the risks and benefits of long-term hormone therapy as it applies to the individual woman. The SWAN study is a cooperative agreement designed to generate collaborative studies representing a broad range of disciplines. The goal of the study is to characterize the biological processes, health effects, psychosocial influences, and sequelae of the pre- to peri- to postmenopausal transition in Caucasian, African American, Chinese, Japanese, and Hispanic women.

Data are being obtained on changing menstrual cycle characteristics, markers of ovarian function, symptoms, demographics, health and social characteristics, diet, race/ethnicity, reproductive history, risk factors for diabetes, hypertension and cardiovascular disease, pre-existing illness, physical activity, and health practices. Menopause and reduced or deficient ovarian function are increasingly believed to play a significant role in the etiology of short- and long-term disorders and diseases. Reduced ovarian hormone levels may play a key role in accelerated bone loss and osteoporosis, and have been associated with cardiovascular disease and other disorders such as urinary incontinence. Both osteoporosis and cardiovascular disease are major causes of frailty, serious disability and mortality, and commonly lead to increased dependency and the need for care in nursing homes.

The **Study of Osteoporotic Fractures (SOF)** is a community-based prospective study in a cohort of 9,704 older women. SOF has comprehensive data about osteoporosis risk factors. Data from SOF have served for: (1) developing osteoporosis guidelines, (2) estimating the cost-effectiveness of screening for osteoporosis, and (3) planning trials of osteoporosis therapies. Preliminary findings suggest that Bone Mineral Density (BMD) may lose predictive value for hip fractures after four-five years. NIA-funded investigators will study the long-term predictive value of BMD, and other risk factors after 10-15 years; substantial declines would strongly affect guidelines concerning the frequency and cost-effectiveness of screening. The investigators recently discovered that women with osteoporosis have a decreased risk of breast cancer, suggesting that these conditions share common etiologies. The investigators will begin the search for these links by investigating whether levels of endogenous sex steroids are associated with breast cancer, and whether other indices of osteoporosis, such as height loss, low ultrasound values, or incident fractures, indicate a lower risk of breast cancer.

Osteoarthritis (OA) and other disorders of the musculoskeletal system are the most frequently reported causes of impairment affecting older individuals in the U.S. OA has been characterized as a slowly evolving degenerative disease affecting cartilage and bone, with many causes. However, because OA has been considered a disease of the elderly, few population-based studies have examined the frequency and characteristics of OA in persons under the age of 45 and consequently the time course and natural history for the development of OA is poorly understood. Furthermore, few studies have focused on non-Caucasian populations. NIA-funded investigators evaluated hand and knee x-rays in 1,053 African-American and Caucasian pre- and peri-menopausal women in southeastern Michigan, 28 to 52 years old, for evidence of OA. The women were participants of the Study of Women's Health Across the Nation (SWAN) or the Michigan Bone Health Study. They also sought to determine the relationship between OA and risk factors such as age, body size, injury, and smoking behavior.

This study provides strong evidence that primary prevention of OA should be attempted in young adulthood to curtail the emergence of radiographically-defined OA at the mid-life. Since radiographically-defined OA affects a substantial proportion of women at midlife, efforts to identify additional risk factors and to improve risk assessment and diagnosis might be appropriately considered for implementation during this time. The striking difference in prevalence of knee OA between African American and Caucasian women, even after adjusting for known risk factors, highlights the need to identify additional factors that affect risk for OA in both these groups.

NIA COLLABORATION WITH OTHER FEDERAL AGENCIES

Many research projects funded by NIA are conducted collaboratively with federal agencies outside of NIH, as well as with other Institutes or Offices of the NIH. Discussed below are some of the agencies NIA works with to support aging-related research.

The **Agency for Healthcare Research and Quality (AHRQ),** formerly the Agency for Health Care Policy and Research, seeks to enhance the quality, appropriateness, and effectiveness of health-care services and to improve access to care. During 2000, the NIA provided funds to the AHRQ for an expert panel meeting, "Improving Functional Health Outcomes in Older People." The meeting was co-sponsored by the John A. Hartford Foundation and the **Centers for Medicare and Medicaid Service (CMS)** (formerly the Health Care Financing Administration (HCFA). In Spring 2001, the NIA, with OBSSR and AHRQ sponsored, a symposium, "Measurement in Diverse Populations Symposium." This symposium is part of the NIA Resource Centers for Minority Aging Research (RCMARs) that support a national effort to increase minority aging research.

The **Centers for Medicare and Medicaid Service (CMS)** administers Medicare, the federal health insurance program for people age 65 and older, and those with certain disabilities. CMS sets eligibility requirements for Medicare recipients, develops claims procedures for health care providers, and regulates the contractors who process Medicare claims. In FY 2000, NIA transferred funds to CMS to support the data processing and logistical arrangements necessary to provide Medicare claims data to NIA's research projects.

Social Security Administration (SSA) funds are supplementing an NIA grant to the University of Michigan to support the Health and Retirement Study (HRS), for data collection and development costs, and to support the work of the HRS Design and Data Monitoring Committee. The surveys are developing longitudinal data on work and retirement, job characteristics, health and disability status, Social Security and private pension benefits, Medicare and other health benefits, economic well-being, and other characteristics related to retirement, health and aging. NIA will provide SSA with copies of materials developed in the performance of this activity, including reports, publications, and survey data tapes.

The **U.S. Census Bureau** is providing funds to NIA to co-fund the **National Academy of Sciences (NAS)** study of race and ethnicity with respect to aging-related issues. This secondary analysis of Census Bureau data will focus on: 1) the nature and extent of racial and ethnic disparities in life expectancy, health, and disability in later life; 2) the extent to which disparities can be attributed to lifestyle risk factors, access to health care, and other biological, social, and economic factors; 3) an examination of immigrant populations who appear to be in better health than mainland Americans of comparable racial and ethnic groups; and 4) recommendations for future research on racial and ethnic disparities. This interagency agreement also will provide the Census Bureau's contribution to the Federal Forum.

The **National Science Foundation (NSF)** conducts "The Panel Study of Income Dynamics (PSID)," a nationally representative longitudinal study that collects information on US households. NIA continues to provide funds to collect additional waves of aging-related data to supplement potential analyses of intergenerational exchanges and interactions. The PSID contains all age groups including the baby boom cohort not yet represented in the Health and Retirement Study (HRS). Specifically, there are approximately 5,000 heads of households and spouses who are baby boomers, born 1945-1964. NIA funding has served to orient the PSID more satisfactorily to aging issues in order to facilitate researchers in merging PSID and HRS data. Researchers are able to use the longitudinal nature of the PSID to explore the potential effect of demographic variables on household wealth accumulation and life course health conditions. Continued data from the PSID will shed light on individual household saving behavior of the baby boom generation and its neighboring age cohorts.

The NIA originally provided funds to the **National Center for Health Statistics (NCHS)** to create the *Longitudinal Study of Aging (LSOA).* This study was based on re-interviewing the age 70 and over respondents to the 1984 Supplement on Aging in 1986, 1988, and 1990. In 1994, NIA provided NCHS with additional funds to create a second LSOA cohort. The LSOA II data, when used in conjunction with data from the original LSOA, enables researchers to track trends in disability and the impact of changes in the health care system on disability. The second follow-up Wave of interviewing, "Wave 3," was completed July 1, 2000. Wave 3 includes a reworking of the Health Care Coverage and Utilization sections, an addition of expectation and engagement questions, and placement of the Childhood Health and Family Longevity section within the main body of the questionnaire.

In FY2000, the NIA provided funds to NCHS to develop a dynamic information system on health and aging using data from NCHS and a number of other data systems, to disseminate this information using modern technologies, to analyze and interpret the information for the **Federal Interagency Forum on Aging-Related Statistics** as well as other consumers, and to train junior researchers. "Trends in Health and Aging Data Warehouse" was released in 1999. Its web URL is: http://www.cdc.gov/nchs/about/otheract/aging/trendsoverview.htm. This compilation of health and aging data uses the statistical software "Beyond 20/20" to produce tables by different topics for five and ten year age groups.

Other aging-related research activities underway at NCHS include the release of several web-based reports including: a) "The Oral Health of Older Americans", b) "The Changing Profile of Nursing Home Residents", c) "Trends in Vision and Hearing Among Older Americans", and d) "Trends in Cause of Death Among the Elderly". Web-based manuscripts or abstracts include: a) "Who Walks in Pain?", Pratt LA, Lentzner, HR., and b) "Eye Care in The Nation's Nursing Homes.", Pratt LA, Gorina Y. NCHS established agreed with CMS to transfer data from the Medicare Current Beneficiary Survey to the Research Data Center at NCHS.

The **US Census Bureau's** *Domestic Aging Program* represents the interests of the NIA and the aging research community, coordinates aging-related activities and materials produced by the Census Bureau, and participates in the Federal Interagency Forum on Aging-Related Statistics. The Program Core activities undertaken in FY2000 include participation in aging-related Census 2000 activities, representation of the Census Bureau at aging-related conferences and meetings, and the production of aging-related materials for dissemination to the public. Census provided several key indicators to the Forum's "Older Americans 2000 – Key Indicators of Well-Being." A profile on the diversity of the older population in the US

has been updated with 2000 Current Population Survey data. The state "Chartbook on Aging" has been completed, and work has begun on the next edition of "65+ in the United States".

In FY 1999, NIA was allocated funds by the NIH **Office of AIDS Research (OAR)** in the Office of the Director (OD) to plan a FY2000 research agenda-setting conference on "Intervention Strategies for Reducing HIV/AIDS Risks in the Older Population" and to update the "HIV/AIDS and Aging" information brochure for the public (one of a series of "Age Pages.") In FY 2000, NIA, in conjunction with NIMH, has entered into an interagency agreement with the **Veteran's Administration** to explore the feasibility of conducting the "Veterans with HIV/AIDS Cohort Study" (VACS).

The NIA jointly issued a RFA with the **National Institute of Occupational Safety and Health (NIOSH)**, the NIH/OBSSR, NIEHS, NIAMS, NICHD, and NIMH entitled, "Health Disparities: Linking Biological and Behavioral Mechanisms with Social and Physical Environments." For this RFA, the physical environment includes physical agents (e.g., radiation), chemical agents (e.g., pesticides) and biological agents (e.g., pathogens and harmful algal blooms) to which individuals are exposed in daily living. The social environment includes individual characteristics (e.g., education, familial factors, coping resources, support systems), community-level characteristics (e.g., residential factors, cultural variables), and institutional and political forces (e.g., racism, classism, media influences). The ultimate goal is to enhance our understanding of the causes and mechanisms responsible for health disparities among the US population, especially between lower and higher socioeconomic status groups. NIA's BSR program is planning a study on the topic of, "Work, Work Organizations, and Older Workers." The input of NIOSH will be sought. NIOSH has begun a panel activity with the Institute on Medicine (IOM) for which NIA is a co-sponsor.

NIA COLLABORATION WITHIN NIH

Biomedical research often falls within the domain of more than one Office or Institute of the NIH. Whenever feasible, the NIA works jointly with these entities to define needed research areas and fund research on aging-related topics. Collaborative activities include joint sponsorship of workshops and conferences, contributions to portions of larger studies sponsored primarily by other Institutes, and co-funding of research projects on a variety of topics. Frequently, the NIA collaborates with other Institutes and Offices to issue PAs or RFAs. Because research related to aging crosses nearly all disciplines and topics pertinent to improvement of public health and determination of cause and prevention of disease, NIA works or has worked collaboratively with every other research entity of the NIH. The lists of Program Announcements under each NIA Program description give a sense of the breadth of NIA's research focus. Current areas of collaboration with other offices or institutes of the NIH include:

- AIDS/HIV prevention and treatment
- Alzheimer's disease
- Arthritis, including osteoarthritis
- Basic research
- Behavioral and social issues in aging
- Bioengineering
- Biology of non-human stem cells
- Bone and the hemotopoietic system
- Cancer and aging
- Caregiving, long-term care, and end-of-life issues
- Cardiovascular and cerebrovascular disorders
- Diabetes
- Genetics and genetic epidemiology
- Diet, nutrition, and caloric restriction
- Exercise, frailty, mobility, and physical fitness
- Heath disparities
- Immunology and vaccines
- Language comprehension changes with aging
- Mental health, mind/body interactions
- Menopause biology
- Minority aging
- Obesity
- Osteoporosis
- Pharmacology and pharmacokinetics in aging
- Neurobiology and neuroinformatics
- Restless leg syndrome
- Sensory aging
- Sleep
- Women's health/families

NIA LEADERSHIP

Richard J. Hodes, M.D.
Director, National Institute on Aging

Dr. Richard J. Hodes, an eminent immunologist, directs the research program of the National Institute on Aging (NIA) at the National Institutes of Health (NIH). The NIA is the principal federal funding agency for studies of the basic, clinical, epidemiological, and social aspects of aging. By promoting the continued development of a strong, diverse, and balanced research program at NIA, Dr. Hodes expects to fuel progress in aging research.

He maintains an active involvement in research on the NIH campus in Bethesda, Maryland, through his direction of the Immune Regulation Section, a laboratory devoted to studying regulation of the immune system, focused on cellular and molecular events that activate the immune response. This involvement in campus research also serves to strengthen ties with other NIH scientists involved in studies of age-related diseases.

Dr. Hodes was named Director of the NIA in 1993, but has enjoyed a long career in science at NIH – first as a clinical investigator in the National Cancer Institute, then as the Deputy Chief and Acting Chief of the Cancer Institute's Immunology Branch.

He is a Diplomate of the American Board of Internal Medicine. In 1995 Dr. Hodes was elected as a member of The Dana Alliance for Brain Initiatives; in 1997 he was elected as a Fellow of the American Association for the Advancement of Science; and, in 1999 he was elected to membership in the Institute of Medicine of the National Academy of Sciences.

Dr. Hodes is a graduate of Yale University. He received his M.D. from Harvard Medical School. As author of more than 200 research papers, he is an influential scientist in and contributor to the field of immunology.

Marcelle Morrison-Bogorad, Ph.D.
Acting Deputy Director, National Institute on Aging

Dr. Marcelle Morrison-Bogorad is Associate Director of the Neuroscience and Neuropsychology of Aging (NNA) Program at the National Institute on Aging (NIA), National Institutes of Health (NIH), Bethesda, Maryland. The NIA is the lead NIH Institute for Alzheimer's disease research. The Program's mission is to develop an understanding of normal brain aging, from genes to cognition, as well as the basis for Alzheimer's disease and other age-related neurodegenerative disorders. The NNA funds an infrastructure network and individual research grants that range from basic science to clinical prevention trials. She serves as spokesperson for the Institute on Alzheimer's disease.

Dr. Morrison-Bogorad obtained an honors degree in Biochemistry from Aberdeen University, Scotland and her Ph.D. in Biochemistry from Glasgow University, Scotland. In her early work, she was one of the first researchers to isolate and study eukaryotic mRNAs. She came to the NIA from the Department of Neurology at the University of Texas Health

Science Center at Dallas, where she was a professor. While in Dallas, Dr. Morrison-Bogorad's research focused on molecular analysis of brain development, Alzheimer's disease, human aging, and the heat shock system in brain. She was a member of the Dallas Alzheimer's Disease Center. She has authored 133 papers, abstracts, book chapters, and invited reviews.

Dr. Morrison-Bogorad was appointed to the Medical and Scientific Advisory Board of the National Alzheimer's Association and served from 1989 to 1996. She served on the Alzheimer's Association Board of Directors from 1994 to 1996. She also was on the Education Committee for the Association for several years. She has given many invited presentations on Alzheimer's disease and the aging brain, both to scientific and lay audiences.

Dan L. Longo, M.D., F.A.C.P.
Scientific Director, National Institute on Aging

Dr. Dan L. Longo, directs the Intramural Research Program of the National Institute on Aging (NIA) at the National Institutes of Health (NIH). Dr. Longo was named Scientific Director of the NIA in 1995 after an outstanding 18-year career at the NIH conducting research in medicine and immunology at both the National Cancer Institute (NCI) and the National Institute of Allergy and Infectious Diseases. His most recent position at the NCI was Director, Biological Response Modifiers Program, and Associate Director, Division of Cancer Treatment, a position he held from 1985-1995.

Dr. Longo is a member of several academic societies. He is a Fellow of the American College of Physicians, and currently serves as Chair of its Oncology Subspecialty Committee. Dr. Longo serves as an associate editor or member of the editorial board of a dozen scholarly journals, including *Journal of the National Cancer Institute, American Journal of Medicine,* and *Blood.* In addition, he is editor of *Harrison's Principles of Internal Medicine, Cancer Chemotherapy and Biotherapy: Principles and Practice, and Clinical Oncology Alert.* He has been listed in every edition of *Best Doctors in America*. Dr. Longo is a Diplomate of the National Board of Medical Examiners, the American Board of Internal Medicine, and is also Board Certified in Medical Oncology (Subspeciality).

Dr. Longo completed medical school at the University of Missouri, Columbia and internal medicine training at the Peter Bent Brigham Hospital and Harvard Medical School in Boston. He is author of more than 660 research papers and book chapters.

STRATEGIC PLAN AND SCIENTIFIC PLANNING PROCESS

Barbara F. Kellner, M.S.

Planning for NIA's Future

The NIA has completed a five-year Strategic Plan for aging research. The plan describes the Institute's mission, areas of current and future research opportunities, and plans for maintaining health and independence for older Americans. The plan includes research goals for fiscal years 2001 through 2005 on the biological, behavioral, and social changes that occur with age and their effects on health and disease, with a special emphasis on preventing Alzheimer's disease. A section of the plan is devoted to research aimed at reducing health disparities among older populations, including rural and minority elderly. The plan is available on the NIA web site (http://www.nih.gov/nia).

The NIA Scientific Planning Process covers a multiyear cycle, but in each year specific key events and components are identifiable. These components are:

- Program Sourcebooks
- NACA Program Reviews
- Planning Group
- Fall/Winter Planning Retreat
- Spring/Summer Planning Retreat
- Working Groups

Program sourcebooks summarize information on the accomplishments, ongoing activities, and plans of each NIA extramural and intramural program. NIA staff use information from sourcebooks throughout the year to prepare reports and respond to inquiries on NIA programs.

At the fall/winter planning retreat, NIA senior management and staff explore implications for the Institute of emerging scientific opportunities. Selected opportunities involving trans-program collaboration are developed and then discussed at the spring/summer planning retreat. The NIA Director's decisions on these initiatives, as well as others submitted by individual programs in the sourcebooks, are discussed with senior Institute staff at a Planning Group meeting and broadly announced as soon as possible after the spring retreat. Working groups composed of representatives of participating programs may be formed to coordinate the implementation of trans-program initiatives. (See timeline of NIA planning activities in the course of a fiscal year on the following page).

Primary goals of the planning process are to:

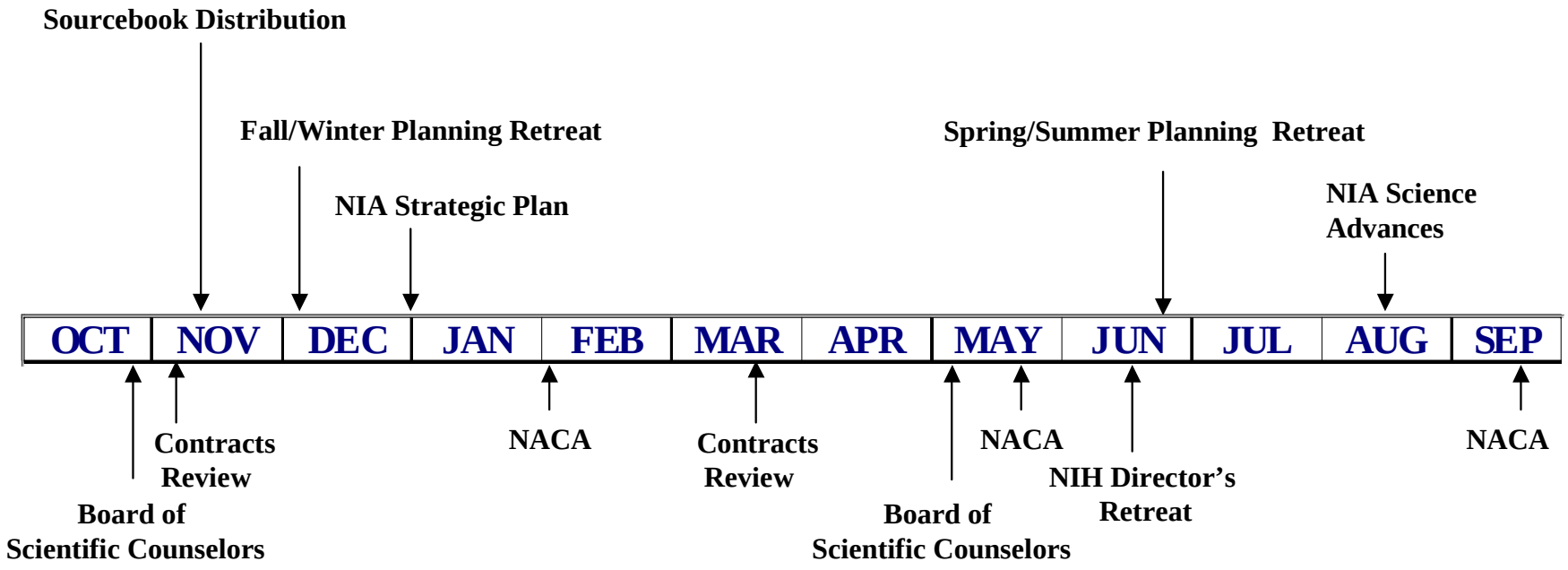
- Identify new and emerging areas of scientific opportunity
- Maintain maximum flexibility to enable the Institute to keep pace with rapid scientific progress
- Improve linkage of planning activities to resource allocation decisions

NIA PLANNING CALENDAR

Key Planning Events

Input from NACA and Board of Scientific Counselors

External Advisory Committees ✦ *State-of-the-Art and Consensus Conferences* ✦ *Sessions at National Meetings*



2001

PUBLIC INFORMATION SERVICES

Jane Shure

The NIA, through its Office of Communications and Public Liaison (OCPL), educates the general public, the research community, physicians, and other health-care providers about aging research and the physical and psychological processes associated with aging. These health communication activities increase public awareness of specific aging issues; reinforce specific knowledge, attitudes, or health behavior; and encourage individual or collective action.

Office of Communications and Public Liaison Activities

To inform the public about NIA's research efforts, OCPL staff members perform a variety of activities to ensure that the American people are kept abreast of the latest advances in the field of geriatric medicine and aging research. These activities include:

- Writing and disseminating newspaper articles, items for technical bulletins, and press releases of the latest medical findings in the field of aging research
- Responding to information requests via letters and distribution of booklets and brochures
- Writing professional education material
- Creating lay-audience fact sheets about specific conditions and illnesses related to aging
- Conducting news conferences and press briefings, and arranging interviews for media outlets
- Publicizing NIA-supported conferences, lectures, and workshops
- Developing and distributing public service announcements
- Maintaining a collection of news clippings, photographs, slides, videotapes
- Using NIA research to increase web accessibility for older people. Creating online learning modules about specific conditions and illnesses related to aging for adults 60 and older .

The OCPL identifies, collects, analyzes, and catalogs science articles for the Alzheimer's disease subfile of the Combined Health Information Database (CHID). At the direction of Congress, NIA established the **Alzheimer's Disease Education and Referral (ADEAR) Center** to respond to a growing need for information about Alzheimer's disease, its impact on families and health professionals, and research into possible causes and cures. It is an information clearinghouse that distributes NIA publications in response to public and professional requests.

- To request information related to Alzheimer's disease, call the ADEAR center at 1-800-438-4380.

- To request information related to other aspects of aging or aging research, call NIA's Information Center at 1-800-222-2225.

INTERNATIONAL ACTIVITIES

Marta Campbell Welsh, M.P.P.

By 2050, more than 20 percent of the world's population will be over age 60, and the number of very old -- those over 85 -- will increase six-fold. As an effect of global aging, non-communicable chronic diseases likely will replace communicable, perinatal, maternal, and nutritional conditions as the world's leading causes of death and disability. These epidemiological predictions highlight a worldwide need to separate chronic disease states from healthy aging, and to develop effective preventive and treatment strategies against the chronic diseases and disabilities often associated with aging.

The NIA Office of International Activities (OIA) serves as a liaison with international agencies, foreign organizations and foreign scientists involved in aging research. It also coordinates aging research activities under agreements between the U.S. and other countries, promotes strategies to build global aging research capacity and supports collaborative research projects. The OIA administers a program that brings foreign scientists to NIA's laboratories to promote collaborative research between NIA's scientists and those in other countries, and to influence the development of biomedical and behavioral research internationally. Sponsoring and participating in international meetings and workshops are also part of the office's responsibilities.

LEGISLATIVE ACTIVITIES

Mary Jo Hoeksema, M.P.A.

The NIA Office of Legislative Activities (OLA) coordinates NIA's participation in congressional hearings, briefing sessions, and symposia on aging-related research, and monitors and analyzes proposed legislation that directly affects the NIA mission and informs NIA staff about its status and implications. This office also serves as the NIA contact for Senators and Representatives and their staff and coordinates responses to congressional inquiries. The Legislative Officer makes and arranges for courtesy calls on members of Congress and their staff who have particular interests in aging research. The office prepares testimony and other presentation materials about aging-related research for congressional hearings and briefings. The office also attends hearings of interest to the Institute and provides summary reports to the NIA Director and appropriate NIA staff. As a related activity, the office also handles congressional correspondence. The office is also responsible for conducting outreach to outside organizations that have an interest in the NIA mission. Recent congressional testimony delivered by NIA officials is posted on the NIA home page at the following URL: http://www.nih.gov/nia/about/legislation/.

OFFICE OF EXTRAMURAL AFFAIRS

Miriam F. Kelty, Ph.D.

The **Office of Extramural Affairs (OEA)** manages NIA's extramural program activities. It often is the first point of contact for applicants requesting information on how to apply for federal support or who wish to know if their research ideas may be of interest to NIA. The OEA coordinates NIA's extramural programs and ensures that policies and procedures are implemented in a uniform and fair way. The Office has responsibility for oversight of grants and contract administration, scientific review, and committee management functions. The Office serves as primary liaison for NIA with the NIH Office of Extramural Research, and with other institutes that share research interests. It also has primary responsibility for NIA's extramural training programs, career development programs, small business initiatives, and other special programs. The Office handles appeals, and scientific integrity and other ethical issues involved in the conduct of research. The OEA organizes meetings of the National Advisory Council on Aging (NACA) and meetings of related groups. Within OEA, the **NIA Training Officer** has central responsibility for the overall direction of research training and career development activities at the institute, including policies related to the types of mechanism supported, the eligibility of particular classes of student and investigator and the structure of research support within the individual mechanisms. The Training Officer develops and manages a series of initiatives to increase the number of underrepresented students and researchers trained in aging research.

The Scientific Review Office (SRO) of the OEA is responsible for initial peer-review of specific research applications assigned to the NIA. These include applications for grants to Centers, for program project initiatives, and for training and career development. Members of NIA's four review panels that correspond to the Institute's program areas and members of the Institute's special emphasis panels include non-government scientists who are themselves grantees and who are expert in the scientific areas of the applications they review.

While the SRO interacts with applicants prior to the award of grants, the **Grants and Contracts Management Office (GCMO)** works with scientists and institutional research administrators to issue, manage, and close awards when the research is completed. GCMO staff members provide guidance on administrative and fiscal policies and practices for the investigator and for the institutional research administrators. For example, they address questions about allowable costs and about major changes in staff or content of the research project. The GCMO has legal responsibility for the fiscal management of the Institute's extramural grants and contracts.

EXTERNAL SCIENTIFIC REVIEW

In support of research, research training, and career development related to aging, the NIA awards grants to universities, hospitals, and research organizations throughout the U.S. and abroad. Approximately 80 percent of the funds appropriated to the NIA are disbursed through these extramural awards. Competition for this funding is very high; for example, over the past ten years, NIA was able to fund fewer than one in three of the research project grant applications it received. To ensure that the research funded is of the highest quality and serves the health needs of the nation, peer review committees comprised of external scientific experts are brought together to review proposed and ongoing research.

Extramural Grant Review

Extramural research investigators trigger the grant review process by submitting grant applications to the NIH Center for Scientific Review (CSR). Initial review of applications may be assigned to a Center review group or to NIA's initial review committee which reviews program project, center, research career, small, and institutional training grant applications, as well as applications submitted in response to RFAs issued by the NIA. Applications clearly within NIA's mandate are forwarded to NIA for funding consideration.

Whether the applications are reviewed at the Center for Scientific Review or at the NIA, committees of experts, including NIH grantees, assess the quality and originality of the proposed science. Reviewers also assess applications for the qualifications of the investigators, quality of the proposed facilities, treatment of animal models, if relevant, and, for research involving humans, the proposed plans for recruiting women and minorities to the studies. The judgment of the group on these parameters is summarized in a report (summary statement) and overall rating (priority score) of the application. These reports are provided to the applicants and to NIA officials. Among the applications assigned to the NIA, approximately the top half, as judged by initial review, are given a second level of review by the National Advisory Council on Aging.

National Advisory Council on Aging

Congress created the National Advisory Council on Aging (NACA) to provide advice on programmatic and policy matters; specifically:

> "to advise, consult with, and make recommendations to the Secretary, DHHS, the Assistant Secretary for Health; the Director, NIH; and the Director, NIA; on matters relating to the conduct and support of biomedical, social, and behavioral research, training, health information dissemination, and other programs with respect to the aging process and the diseases and other special problems and needs of the aged."

Grant applications over $50,000 must receive Council approval to be eligible for funding. In its deliberations, the NACA reviews summary statements to evaluate the fairness and appropriateness of the initial review of grant applications, and considers the scientific and public importance of the proposed work. In cases in which the applicant or NIA staff has concerns about the initial review of the application (special actions), NACA members can evaluate these concerns.

Council members also serve as a conduit for insights into the concerns and opinions of the research community, and assist in keeping the scientific community, Congress, and the public knowledgeable about the activities of the NIA.

The NACA meets three times each year, typically for a period of two days to review applications for grants and cooperative agreements for research and training. The group recommends funding of research applications that show significant promise of a) improving the quality of life and health care for the aged; or b) making valuable contributions to our scientific knowledge of the aging process.

The NACA consists of 18 members appointed by the DHHS Secretary and 5 non-voting *ex officio* members. Of the 18 appointed members, 12 are leading representatives of the health and scientific disciplines and are leaders in the fields of public health and the behavioral or social sciences relevant to the activities of the NIA, particularly with respect to biological and medical sciences relating to aging and public health. Six of the members are leaders from the general public in the fields of public policy, law, health policy, economics, and management. Members are invited to serve for overlapping four-year terms.

Once the Council provides its recommendations, the NIA Director may approve payment of applications that have been favorably reviewed and for which sufficient funds are available. Primary weight is given to the scientific quality of the application as judged by initial peer review. Consideration is also given to the proposed research's relevance to NIA priorities and to the timeliness of the research.

MEMBERSHIP ROSTER
NATIONAL ADVISORY COUNCIL ON AGING
NATIONAL INSTITUTE ON AGING

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INTRAMURAL SCIENTIFIC REVIEW

The investigators and projects of the Intramural Research Program (IRP) are reviewed on a regular basis for quality and productivity by NIA's Board of Scientific Counselors (BSC). Past performance as well as future research plans are included in the review, as are issues affecting recruitment and retention of scientists. A review of each of the laboratories of the IRP takes place every four years on a rotating basis.

The BSC consists of nine members with outstanding scientific credentials who are charged to provide rigorous and objective on-site reviews. New BSC members are appointed by the Director, NIH, based upon recommendations from current BSC members, the NIA Scientific Director, the NIA Director, and the NIH Deputy Director for Intramural Research. The BSC advises the NIH Director and Deputy Director for Intramural Research, and the NIA Director and Scientific Director. BSC members are invited to serve for overlapping terms of five years. At times, *ad hoc* external reviewers may supplement the BSC membership.

The Institute annually provides a written report to the NACA that describes research reviewed by the BSC and the results of that review. Based upon this report, the NACA may make recommendations to the NIA Director regarding such research.

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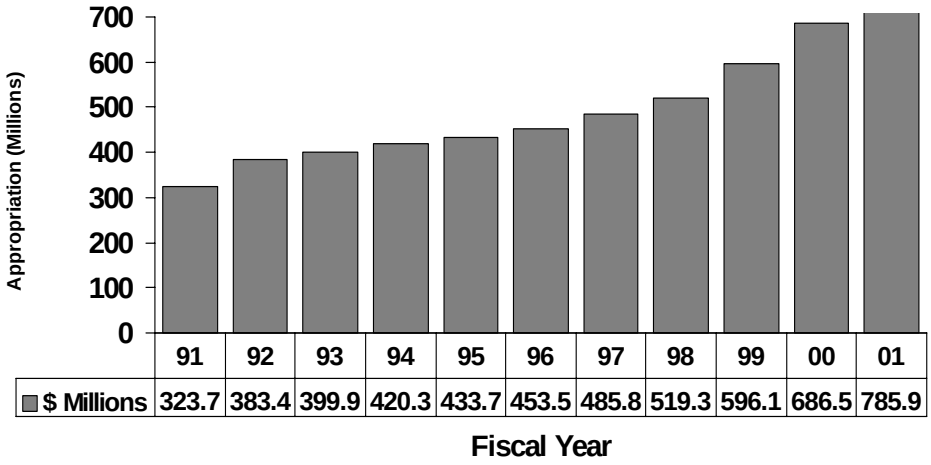
NIA FUNDING AND RESEARCH SUPPORT MECHANISMS

This section includes three graphics and one table to give the reader a concise overview of the funding and budget aspects of the NIA.

- Trends in Appropriations Fiscal Years 1991-2001
- Research Project Grant Success Rates Fiscal Years 1990-2000
- Distribution of Obligations by Budget Category Fiscal Year 2000
- Actual Obligations for Fiscal Year 2000

National Institute on Aging

Trends in Appropriations
Fiscal Years 1991 - 2001



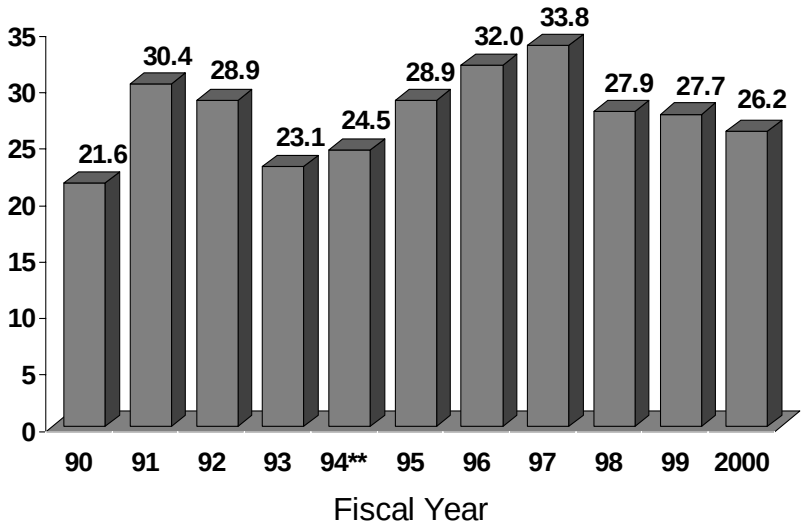
Source: NIA Budget Office
January 2001

Trends in Appropriations. The United States Congress holds appropriations hearings in the Spring of each year, and determines the funding level for each NIH Institute for the upcoming fiscal year. NIA appropriations have risen steadily each year, from $323.7 million in fiscal year 1991 to $785.9 million in fiscal year 2001.

National Institute on Aging

Research Project Grant Success Rates*

Fiscal Years 1990 –2000



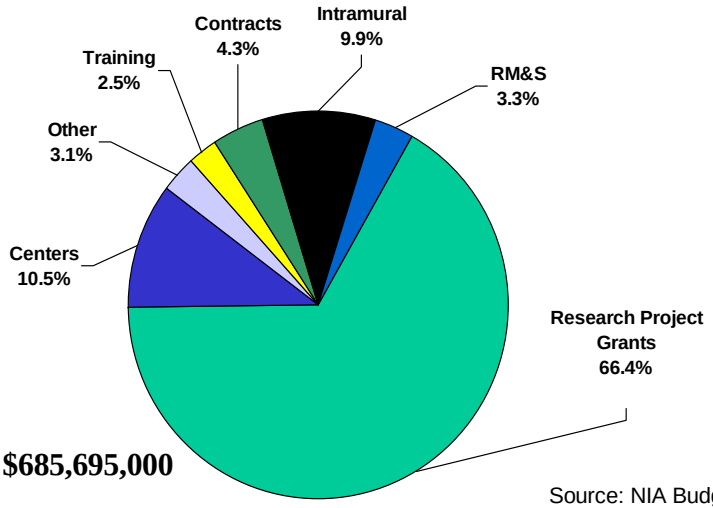
* Success rate: Ratio of applications awarded to applications reviewed.

** Beginning in Fiscal Year 1994, SBIR and STTR applications are not included in Success Rate calculations.

Source: NIA Budget Office
January 2001

Research Project Grant Success Rates. Research project grants continue to be the highest NIH funding priority, since it is through this mechanism that investigator-initiated research is supported. This chart shows a history of the proportion of NIA applications reviewed that were actually awarded funds from 1990 through 2000.

National Institute on Aging
Distribution of Obligations by Budget Category
Fiscal Year 2000



Total, NIA: $685,695,000

Source: NIA Budget Office
January 2001

Distribution of Obligations by Budget Category. Financial obligations are commitments by a government agency to pay a sum of money. This pie chart shows NIA's distribution of financial obligations by budget category for fiscal year 2000. By far, the largest portion of NIA's budget goes to fund extramural activities, which include research project grants, research centers, and research training.

National Institute on Aging

ACTUAL OBLIGATIONS FOR FISCAL YEAR 2000

Mechanism	Number of Awards	Dollars (Thousands)
RESEARCH GRANTS		
Research Project Grants:		
Non-competing	741	$296,268
Admin. Supplements	116	8,956
Competing		
Renewals	79	44,681
New	305	89,916
Supplements	10	754
Subtotal, Competing	**394**	**135,351**
Subtotal, RPGs	**1,135**	**440,575**
SBIR/STTR	55	15,006
Total, Research Project Grants	**1,190**	**$455,581**
Research Centers:		
Special/Competing	**66**	**$ 71,770**
Other Research:		
Research Careers (K awards)	158	15,561
Coop. Clinical Research	3	1,616
Minority Biomedical Research Support	0	1,173
Other Related Research	27	2,600
Total, Other Research	**188**	**$ 21,010**
TOTAL, RESEARCH GRANTS	**1,444**	**$548,361**
TRAINING		
Individual	52	1,752
Institutional (FTTPs)	449	15,557
TOTAL, TRAINING	**551**	**$ 17,309**
R&D CONTRACTS	61	29,641
INTRAMURAL RESEARCH		67,574
RESEARCH MANAGEMENT & SUPPORT		22,810
GRAND TOTAL, NIA		**$685,695**

Note: Includes AIDS

Source: NIA Budget Office
January 2001

NIA EXTRAMURAL AWARD MECHANISMS

The major portion of NIA's budget is used to fund research, training, and career development outside of the NIH. NIA's extramural programs support a variety of research project, career development, and training grant mechanisms appropriate for individuals at different stages of their careers. For most research grant mechanisms, investigators must be conducting research at the postdoctoral level. Training awards are made both to postdoctoral and predoctoral applicants. Career development awards are designed to enable researchers to begin their careers as well as to assist mid-career and senior investigators in augmenting their skills. There are also mechanisms that support multidisciplinary teams of researchers or that involve cooperation among three or more investigators addressing a common theme.

Research Grants are the largest category of NIH and NIA research funding. Grants are awarded to nonprofit and for-profit organizations, universities, hospitals, research foundations and agencies. Programs such as the Small Business Innovation Research grants (SBIR), Academic Research Enhancement Awards (AREA), and Minority Access to Research Careers (MARC) grants have been established for certain categories of applicants. Several programs are aimed specifically at encouraging minorities and women to participate in research.

The NIA-supported mechanisms described below are grouped into three categories: a) research project grants, b) research centers, and c) other research award mechanisms (e.g., career development, and other research-related programs).

Research Project Grants (RPG)

Traditional Research Projects (R01) support a principal investigator's work on a discrete research project. The R01 is the traditional mechanism through which much of NIA's extramural research is supported. Some of these areas of research are listed as Program Announcements (PA) at the end of each extramural program description in this guide.

Small Research Grants (R03) provide research support specifically limited in time and amount for studies in categorical program areas. These grants are generally for preliminary short-term projects or secondary data analyses and are nonrenewable.

Research Program Projects (P01) support broadly-based, often multidisciplinary, research programs involving groups of investigators working on research projects that together contribute to the overall program objective.

Exploratory/Developmental Planning Grants (R21) encourage the development of new research activities in categorical program areas. Support generally is restricted in level of support and in time.

SBIR Grants (R43 and R44) support projects to establish the technical merit and feasibility of research and development ideas that may ultimately lead to commercial products or services.

STTR Grants (R41 and R42) support cooperative research and development projects between small business concerns and research institutions to establish the technical merit and feasibility of ideas that have potential for commercialization.

Method to Extend Research in Time (MERIT, R37) awards provide long-term support to outstanding, experienced investigators. MERIT awards are initiated by NIA and by the National Advisory Council on Aging (NACA).

Academic Research Enhancement Awards (AREA, R15) support scientists at institutions that are not research-intensive, but train a significant number of research scientists on small-scale, health-related research projects.

Cooperative Agreements (U01) support discrete research involving extramural investigators in which institute staff play a substantial role. Clinical trials are sometimes supported through cooperative agreements.

Research Centers

Research Center Grants (P20, P30, P50, and P60) support multidisciplinary research and development programs. Research centers often have a clinical orientation and are usually developed in response to an NIA announcement requesting research in a specific area of need.

Other Award Mechanisms

Conference Grants (R13/U13) support recipient-sponsored and directed international, national, or regional meetings, conferences, and workshops. The U13 is used when NIA staff play a substantial role in the organization or presentation of the event.

Education Projects (R25) provides support to develop and/or implement a program as it relates to a category in one or more of the areas of education, information, training, technical assistance, coordination, or evaluation.

Research and Development Contracts (N01) are negotiated with qualified domestic and foreign organizations to support basic, applied, or developmental research; and to test or evaluate a product, material, device, or component for use by the research community. The initiative for this research generally originates within NIA.

Career Development Awards. The NIA supports the following awards aimed at the development of outstanding research scientists:

Mentored Research Scientist Development Awards (K01) are early or mid-career awards for individuals with some prior postdoctoral research experience. These awards are for research scientists who need an additional period of sponsored research experience to gain expertise in a new research area, or in an area that would demonstrably enhance the candidate's scientific career.

Independent Scientist Awards (K02) are early to mid-career awards for individuals with prior grant funding who seek to become leaders in their research fields. This “time

off from teaching" award provides support for newly independent scientists who can demonstrate the need for a period of intensive research to enhance their research careers.

Academic Career Awards (K07) are "Leadership" awards. These awards are for acknowledged research leaders who wish to build aging research, or an aspect of aging research, at their institutions. The K07 provides support for individuals interested in introducing or improving curriculum to enhance the educational or research capacity of an institution. The award supports junior candidates who wish to develop expertise by improving teaching, research, and leadership skills. It also supports senior candidates with demonstrated scientific expertise and leadership skills.

Mentored Clinical Scientist Development Awards (K08) are for junior clinicians with little-to-moderate research training who wish to become independent clinician-scientists. This mechanism provides specialized study for clinically trained professionals who are committed to a career in research and have the potential to develop into independent investigators. The award supports a three-, four-, or five-year period of supervised research experience that may integrate didactic studies with laboratory or clinically-based research.

Mentored Clinical Scientist Development Program Awards (K12) are made to an educational institution to support career development experiences leading to research independence for clinically trained individuals. Under this award, newly trained clinicians are selected and appointed by the grantee institution. The research experience of the candidates selected for support under this award is similar to that supported by the individual Mentored Clinical Scientist Development Award.

Mentored Patient-Oriented Research Career Development Awards (K23) are for junior clinicians with little-to-moderate research training who wish to become independent clinician-scientists trained in patient-oriented research. It is similar to the K08 in that it is designed to train aspiring clinician-scientists to become independent researchers. The major difference is that investigators under this mechanism must focus on patient-oriented research which includes 1) mechanisms of human disease; 2) therapeutic interventions; 3) clinical trials, and; 4) development of new technologies.

Mid-Career Investigator Award in Patient-Oriented Research (K24) are for mid-career clinician-scientists who wish to devote more time to patient-oriented research and to mentoring junior clinicians in patient-oriented research. Clinical researchers who are no more than 15 years beyond their specialty training, and who have active research support, may use the award to take time off from clinical or administrative duties to pursue patient-oriented research and to mentor junior clinician.

Mentored Quantitative Research Career Development Award (K25). (Postdoctoral Individuals/New Independent Researchers.) This program fosters interdisciplinary collaboration for scientists and engineers with little or no biomedical or behavioral research experience who are committed to establishing themselves in careers as independent biomedical or behavioral investigators. This mechanism is aimed at research-oriented junior faculty scientists or engineers (e.g., early to mid-levels of assistant professor or research assistant professor ranks).

Midcareer Investigator Award in Mouse Pathobiology Research (K26). This award provides support for established pathobiologists to allow them protected time to devote to mouse pathobiology research and to act as mentors for beginning investigators. Target candidates are outstanding pathobiology researchers who are within 15 years of their specialty training, who can demonstrate the need for a period of intensive research focus as a means of enhancing their research careers, and who are committed to mentoring the next generation of mouse pathobiologists. NIA cosponsors this announcement with the National Center for Research Resources (NCRR).

Clinical Research Curriculum Awards (K30) give institutions support to develop or expand clinical research curricula. NIA encourages applicants to build curricula in clinical geriatric research. The curricula must be two years in duration although the awards are for five years and are renewable.

Research Training Awards

Training awards support the research training of scientists for careers in the behavioral and biomedical sciences, as well as help professional schools to establish, expand, or improve programs of continuing professional education. Training awards consist of institutional training grants (T's) and individual fellowships (F's). The primary training mechanisms are National Research Service Award (NRSA) institutional training grants and fellowships, and awards specifically targeted for minority institutions and minority scientists.

Institutional Training Grants include:

Institutional National Research Service Awards (T32) enable institutions to make awards to individuals selected for predoctoral and postdoctoral research training in specified areas. This T32 provides 5 years of support to grantee institutions for research training programs for physicians who have completed one or more years of clinical fellowship training in geriatrics.

Short-Term Research Training Awards (T35) provide individuals with research training during off-quarters or summer periods to encourage research careers and/or research in areas of national need.

Individual Fellowships include:

Postdoctoral Individual National Research Service Awards (F32) provide postdoctoral research training to individuals to broaden their scientific background and extend their potential for research in specified health-related areas.

National Research Service Award for Senior Fellows (F33) provide opportunities for experienced scientists to make major changes in the direction of their research careers, to broaden their scientific background, and to acquire new research capabilities. Developed a few years ago, the award allows senior researchers to take time from regular professional responsibilities for the purpose of increasing capabilities to engage in health-related research.

Training Opportunities for Special Populations

NIA supports a number of special-purpose initiatives on training in aging research that are designed to increase the numbers of trained researchers from minority populations, underrepresented ethnic groups, among people with disabilities, and among individuals who have been forced to interrupt research careers. The first two mechanisms below, the MARC-T4, and the MARC-T36, are funded by the National Institute of General Medical Sciences (NIGMS). The NIA co-funds subprojects that are relevant to aging research.

Minority Access to Research Careers (MARC-T34) are Undergraduate Institutional grants that enable minority institutions to grant awards to individuals selected for undergraduate research training in the biomedical and behavioral sciences.

MARC Visiting Professors for Minority Institution Awards (MARC-T36) are designed to increase the number of well-trained minority scientists in biomedical disciplines and to strengthen the research and teaching capabilities of minority institutions. Training mechanisms include visits by experienced scientists to minority institutions, and workshops/conferences designed to enhance the research training experience of students/faculty from minority institutions.

Minority Supplement Awards for Students and Investigators. These awards support high school students through junior faculty members for a minimum of one year and up to four years. These awards give principal investigators an administrative supplement to support a minority student or investigator on the grant in order to advance the student's or investigator's research career.

Minority Pre-doctoral Fellowships (F31). NIA participates in this general NIH initiative that can support minority students at any stage of their predoctoral career. These awards grant a stipend with a periodic cost-of-living increase for up to five years for predoctoral minority students. Tuition and fees are also partially covered.

Predoctoral Individual Fellowship Awards for Students with Disabilities. NIA participates in this general NIH initiative that can support students with disabilities at any stage of their predoctoral career.

Research Supplement Awards for Students and Investigators with Disabilities. NIA participates in this NIH general initiative that permits principal investigators an administrative supplement to support a student or investigator with disabilities on the grant in order to advance the individual’s research career.

Re-Entry Supplements for Investigators Forced to Interrupt Their Career. NIA participates in this general NIH initiative that permits principal investigators on many different kinds of research grants an administrative supplement to support an individual returning to the research work force after a forced interruption (such as raising children or caring for a disabled parent).

Minority Dissertation Research Grants in Aging (R03). These awards support dissertation research on aging for doctoral candidates from racial or ethnic groups underrepresented in biomedical or behavioral research.

Training Grant (T32) Add-on Slots. These awards are for minority doctoral students for up to two years. Funding is the same as for pre-doctoral fellowships.

Minority Supplements to MERIT Awards (R37). These awards enable a senior investigator to mentor and train a minority scientist. The awards, up to $5,000 per year, are for high school students through junior faculty. MERIT supplements can run for three years.

Minority Biomedical Research Support (MBRS) and Minority Access to Research Careers (MARC) Awards. Support at minority-serving 2-4 year colleges and universities for outstanding minority students and faculty who plan to pursue graduate programs leading to the Ph.D. degree in health-related sciences.

Other Training Opportunities

Summer Institute on Aging Research. This annual, one-week event provides junior investigators an opportunity to learn about the substance and methodology of aging research from recognized experts in the field. The goal is to enhance participants' potential for success as independent investigators. Racial and ethnic minority investigators and researchers interested in research on minority health are especially encouraged to apply.

Technical Assistance Workshop. With financial support from the NIH Office of Research on Minority Health, the NIA sponsors an intensive two-day workshop each year on the research grant application process for minority investigators and for scientists with a commitment to ethnic/minority aging research.

Regional Training Meetings. These meetings inform faculty, students, and administrators of racial and ethnic minority groups about NIA programs. In addition to disseminating information, the regional meetings obtain reactions to ongoing programs and information on research training needs in the various regions.

NIA INTRAMURAL TRAINING MECHANISMS

The Intramural Research Program has several mechanisms to train high-quality researchers in biomedical and behavioral aging-related research:

Postdoctoral Fellow. A Postdoctoral Fellow is a trainee who participates in laboratory-based or population-based biomedical research for the purpose of obtaining advanced training under the direction of a senior member of the scientific staff. Scientists who have less than five years of postdoctoral experience are eligible for this program and may remain in the program for a maximum of five years.

- **Intramural Research Training Award (IRTA).** The NIH Postdoctoral IRTA Program, available to U.S. citizens, provides advanced training and research experience to physicians and Ph.D.-level investigators who are at the beginning stages of their professional research careers. Participants will engage in research studies under the direction of preceptors, and will apply their newly-gained knowledge and enhance their research skills by participating in on-going research investigations.

- **Visiting Fellows (VF)**. The NIH Visiting Program for foreign scientists is composed of two different types of awards at varying stages of a researcher's career. The **Visiting Fellowship** is an award to a foreign scientist, with 5 years or less of relevant postdoctoral research experience, offering advanced research experience and training and not requiring the performance of services for the NIH. The **Research or Clinical Fellowship** requires an FTE and the performance of services for the NIH. These appointments are for scientists with 3 or more years of relevant postdoctoral experience.

Research Fellow. A Research Fellow is an NIH scientist with a doctoral degree. The purpose of a Research Fellowship is to provide junior-level scientists with doctoral degrees experience in biomedical research while they provide a service relevant to the NIH's program needs. The Research Fellow will spend the entire fellowship in laboratory research, while supporting the performance of NIH intramural research. The appointment gives the fellow experience in laboratory-based or population-based biomedical research.

Clinical Fellow. Clinical Fellow is a doctoral-level health professional with interest in biomedical research relevant to NIH program needs. The purpose of a Clinical Fellowship is to provide junior-level physicians experience in biomedical research relevant to NIH's program needs. This position has both clinical and laboratory components, with some time spent in direct patient contact supporting the performance of clinical protocols and the rest in laboratory research related to these protocols. In some cases, Clinical Fellows may receive approved credit towards residency training, advanced subspecialty training, or Board certification.

Special Volunteers. This mechanism allows interested volunteers to gain valuable training while performing volunteer service to a particular laboratory. Special Volunteers are entitled to compensation for injuries, to protection under the Federal Tort Claims Act, and to receive royalties for inventions. Training for Special Volunteers may be supported by the NIH. The Volunteer authority may be used to appoint postdoctoral investigators who are supported by outside grants.

Students. Registered students (at all levels from high school through graduate, medical or dental school) are offered a range of research training programs at NIH. The purpose of the student research programs is to enhance a student's knowledge and understanding of biomedical research and to contribute to the achievement of a student's educational goals.

To Contact the NIA…

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Office of Extramural Affairs	
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Intramural Research Program Dan Longo, M.D., Scientific Director	GritheP@grc.nia.nih.gov 410-558-8110

Additional NIA offices and Web sites about aging and health:

Office of Communications and Public Liaison	KarpF@nia.nih.gov 301-496-1752
Office of International Activities	WelshM@nia.nih.gov 301-496-0767
Office of Legislative Analysis	HoeksemM@nia.nih.gov 301-496-0261
Office of Planning, Analysis, and Evaluation	KellnerB@nia.nih.gov 301-496-3121
NIA Information Center	niainfo@access.digex.net 1-800-222-2225 1-800-222-4225 (TTY)
Alzheimer's Disease Education and Referral Center (ADEAR Center)	adear@alzheimers.org 1-800-438-4380 301-495-3333 (Fax) http://www.alzheimers.org/adear
NIA World Wide Web Page	http://www.nih.gov/nia
NIH World Wide Web Page	http://www.nih.gov
NOTES: ***To obtain contact information for other NIH/NIA staff:***	http://directory.nih.gov
To address e-mail to NIH staff, the following convention may be used:	**firstname.lastname@nih.gov** **Example: james.shannon@nih.gov**

GLOSSARY OF ACRONYMS

ACTIVE	Advanced Cognitive Training for Independent and Vital Elders
AD	Alzheimer's Disease
ADC	Alzheimer's Disease Centers
ADCC	Alzheimer's Disease Core Centers
ADCS	Alzheimer's Disease Cooperative Study
ADEAR	Alzheimer's Disease Education and Referral Center
ADL	Activities of Daily Living
ADRC	Alzheimer's Disease Research Centers
AHRQ	Agency for Healthcare Research and Quality
AIDS	Acquired Immunodeficiency Syndrome
ALS	Amyotrophic Lateral Sclerosis
APP	Amyloid Precursor Protein
AREA	Academic Research Enhancement Awards
BAP	Biology of Aging Program
BLSA	Baltimore Longitudinal Study on Aging
BMAP	Brain Molecular Anatomy Project
BMD	Bone Mineral Density
BPH	Benign prostatic hyperplasia
BSC	Board of Scientific Counselors
BSR	Behavioral and Social Research Program
CC	Warren Grant Magnuson Clinical Center
CDC	Centers for Disease Control and Prevention
CHAMPS-II	Community Health Activities Model Program for Seniors
CHID	Combined Health Information Database
CMS	Centers for Medicare and Medicaid Services
CNS	Central nervous system
CR	Caloric restriction
CSR	Center for Scientific Review
CVD	Cardiovascular disease
DHEA	Dehydroepiandrosterone
DHHS	Department of Health and Human Services
DNA	Deoxyribonucleic acid
EPESE	Established Populations for Epidemiologic Studies of the Elderly
ER	Estrogen receptor
FDA	Food and Drug Administration
FTE	Full-Time Equivalent (personnel)
FTTP	full-time training position
FY	Fiscal Year: October 1-September 30
GCMO	Grants and Contract Management Office
GP	Geriatrics Program
GRC	Gerontology Research Center
HAAS	Honolulu-Asia Aging Study
HANDLS	Healthy Aging in National Diverse Longitudinal Samples Study
HIV	Human Immunodeficiency Virus
HRS	Health and Retirement Study
HRSA	Health Resources and Services Administration
IADL	Instrumental Activities of Daily Living
ICPSR	Inter-University Consortium for Political and Social Research
IGF-I	Insulin-like growth factor-I
IOM	Institute of Medicine
IRP	Intramural Research Program
IRTA	Intramural Research Training Award
JAMA	The Journal of the American Medical Association
LAG	Longevity assurance gene
LEDB	Laboratory of Epidemiology, Demography, and Biometry
LCMB	Laboratory of Cellular and Molecular Biology
LCI	Laboratory of Clinical Investigation
LCS	Laboratory of Cardiovascular Science
LG	Laboratory of Genetics
LI	Laboratory of Immunology
LMG	Laboratory of Molecular Genetics
LNS	Laboratory of Neurosciences
LPC	Laboratory of Personality and Cognition
LSOA	Longitudinal Study of Aging
MARC	Minority Access to Research Careers Program
MBRS	Minority Biomedical Research Support Program
MCI	Mild cognitive impairment
MDS	Minimum Data Set
MERIT	Method to Extend Research in Time Award
MRI	Magnetic resonance imaging
mtDNA	mitochondrial deoxyribonucleic acid
NACA	National Advisory Council on Aging
NACC	National Alzheimer's Coordinating Center
NACDA	National Archive of Computerized Data on Aging
NAS	National Academy of Sciences
NCCAM	National Center for Complementary and Alternative Medicine
NCHS	National Center for Health Statistics
NCI	National Cancer Institute
NCRR	National Center for Research Resources
NEI	National Eye Institute
NHGRI	National Human Genome Research Institute
NHLBI	National Heart, Lung, and Blood Institute
NIA	National Institute on Aging
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIAID	National Institute of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NICHD	National Institute of Child Health and Human Development
NIDA	National Institute on Drug Abuse
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDCR	National Institute of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NINDS	National Institute of Neurological Disorders and Stroke
NINR	National Institute of Nursing Research
NIOSH	National Institute of Occupational Safety and Health
NLM	National Library of Medicine
NLTCS	National Long Term Care Survey
NNA	Neuroscience and Neuropsychology of Aging Program
NRC	National Research Council
NRSA	National Research Service Award
NSF	National Science Foundation
OA	Osteoarthritis
OAICs	Claude D. Pepper Older Americans Independence Centers

GLOSSARY OF ACRONYMS

OAR	Office of AIDS Research
OBRRD	Office of Biological Resources and Resource Development
OBSSR	Office of Behavioral and Social Sciences Research
OCPL	Office of Communications and Public Liaison
OD	Office of the Director
OEA	Office of Extramural Affairs
OECD	Organization for Economic Cooperation and Development
OIA	Office of International Activities
OLA	Office of Legislative Activities
OPAE	Office of Planning, Analysis, and Evaluation
ORRD	Office of Research Resources and Development
ORWH	Office of Research on Women's Health
PA	Program Announcement
PET	Positron emission tomography
PS 1	Presenlin 1
PSID	Panel Study of Income Dynamics
R&D	Research and Development
RCMAR	Resource Centers for Minority Aging Research
REACH	Resources for Enhancing Alzheimer's Caregiver Health
RFA	Request for Applications
RFP	Request for Proposals
RM&S	Research Management and Support
RPG	Research Project Grant
SAG	Senescence assurance genes
SBIR	Small Business Innovation Research
SCN	Suprachiasmatic nucleus
SCU	Special Care Unit
SES	Socioeconomic status
SOF	Study of Osteoporotic Fractures
SRO	Scientific Review Office
SSA	Social Security Administration
STTR	Small Business Technology Transfer
SWAN	Study of Women's Health Across the Nation
VA	Veteran's Administration
VACS	Veteran's with HIV/AIDS Cohort Study
WHAS	Women's Health and Aging Study
WHO	World Health Organization

GLOSSARY OF TERMS

Activities of Daily Living (ADL) -ADL's are essential tasks of daily life such as bathing, dressing, using the toilet, and getting in and out of chairs.

Appropriations - An act of Congress that allows federal agencies to incur obligations and make payments from the Treasury for specified purposes. An appropriation usually follows enactment of authorizing legislation and is the most common means of providing budget authority. Appropriations do not represent cash actually set aside in the Treasury for purposes specified in the appropriation act; they represent limitations of amounts that agencies may obligate during the period of time specified in the respective appropriation acts. At the NIH, each Institute and Center receives its own appropriation.

Competing Applications - New applications and those competing for renewal.

Constant Dollars - Current dollars for a fiscal year adjusted for inflation with reference to a base year, according to the Biomedical Research and Development (R&D) Price Index.

Extramural Research – Research performed by investigators outside the NIH and supported by the NIH. It includes grants, cooperative agreements, or contracts from NIH to scientific investigators or organizations in support of biomedical or behavioral research and research training related to health and disease.

Fiscal Year (FY) - Any yearly accounting period, without regard to its relationship to a calendar year. The fiscal year for the federal government begins October 1 and ends the following September 30. (For example, FY 2000 covers the period October 1, 1999 – September 30, 2000).

Instrumental Activities of Daily Living (IADL) - IADLs are more complex than ADLs. (See above). IADLs are activities that require sequential actions and/or planning. Examples include preparing meals, shopping, and cleaning.

Initiative - Research activities of NIH Institutes such as workshops, Program Announcements (PA), Request for Applications (RFA), Request for Proposals (RFP) or other mechanisms that support biomedical or behavioral research or research training.

Intramural Research -Research performed by investigators within the NIH community or extensions thereof.

NIH Guide to Grants and Contracts - The NIH Guide announces scientific initiatives in the form of PAs, RFAs, and RFPs and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by NIH.

Obligations - Commitments by a government agency to pay a particular sum of money for orders placed, grants and contracts awarded, services received, and similar transactions during a given period of time.

Program Announcement (PA) -PAs are issued by one or more NIH Institutes to stimulate research in specific areas for which grant applications are invited. PAs are published in the "NIH Guide to Grants and Contracts," and are intended to encourage research in stated topics. Unlike RFAs, PAs do not have an expiration date and do not have funding set aside for specific period of time. Meritorious applications sent in response to PAs are funded based on successful peer review and availability of funds.

Request for Applications (**RFA**) **-** Invites applicants to apply for a research grant in a specific scientific area. The RFA has a designated submission date and funds set aside for a certain number of awards.

Research Management and Support (RM & S) - Management of extramural programs, Office of the Director, and certain management costs applicable to over operations.

Request for Proposals (RFP) - Solicits contracts from for-profit organizations to acquire specific services or products. Research contract awards may be made for the development and support of research resources, data resources, or for the conduct of research that fulfills a specific research need.

Success Rates – Ratio of applications awarded to applications reviewed.